Federal Register

Thursday
September 1, 1994

## Part III

# Environmental Protection Agency

**40 CFR Parts 700, 720, 721, 723, and 725**
**Microbial Products of Biotechnology; Proposed Regulation Under the Toxic Substances Control Act; Proposed Rule**

## ENVIRONMENTAL PROTECTION AGENCY

## 40 CFR Parts 700, 720, 721, 723, and 725

**[OPPTS–00049c; FRL–4778–4]**

RIN 2070–AB61

# Microbial Products of Biotechnology; Proposed Regulation Under the Toxic Substances Control Act

**AGENCY:** Environmental Protection Agency (EPA).

**ACTION:** Proposed rule.

**SUMMARY:** EPA is proposing this regulation under section 5 of the Toxic Substances Control Act (TSCA), 15 U.S.C 2604, to screen microorganisms before they are introduced into commerce. Under an interpretation EPA issued in 1986 (51 FR 23302, June 26, 1986), ''new'' microorganisms are those formed by deliberate combinations of genetic material from organisms in different genera. This proposed rule is designed to prevent unreasonable risk to human health and the environment without imposing unnecessary regulatory burdens on the biotechnology industry. This proposed regulation describes notification procedures and microorganisms that would be exempt from notification.

**DATES:** Written comments on this proposed rule should be received by October 31, 1994.

EPA may hold an informal hearing in Washington, DC, if EPA receives written requests to hold a public hearing. For further information on the hearing, see Unit IV.I. of this preamble. Written requests to make an oral presentation should be submitted to the Environmental Assistance Division by October 3, 1994. Persons are advised to call the Environmental Assistance Division after October 11, 1994 to ascertain if a hearing is to be held, and the date, time, and location.

**ADDRESSES:** Comments on issues concerning this proposed rule should bear the docket control number OPPTS–00049C, and should be submitted to the following address: Document Processing Center (7407), Office of Pollution Prevention and Toxics, Environmental Protection Agency, Rm. L–100, 401 M St., SW., Washington, DC 20460.

**FOR FURTHER INFORMATION CONTACT:** For general information including copies of this document and related materials: Susan Hazen, Director, Environmental Assistance Division (7408), Office of Pollution Prevention and Toxics, Environmental Protection Agency, Rm. EB–44, 401 M St., SW., Washington, DC 20460, In the USA: (202–554–1404), TDD: (202–554–0551). For technical information regarding this document: Paul Campanella, Office of Pollution Prevention Toxics (7405), Environmental Protection Agency, Rm. E-611, 401 M St., SW., Washington, DC 20460, In the USA: (202–260–3725).

**SUPPLEMENTARY INFORMATION:** The preamble accompanying this proposed rule is divided into the following Units:

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## I. Introduction

### *A. Purpose of This Proposed Rule*

This document proposes procedures for EPA to screen new microorganisms. EPA's goals in proposing these rules are to take into account scientific uncertainties surrounding the behavior of these microorganisms and avoid unreasonable risks to health and the environment which may be associated with their use, to avoid imposing unwarranted costs and restrictions on a promising industry, and to establish a flexible review program that can adjust as the technology evolves and matures.

EPA will screen new microorganisms before they are manufactured for general commercial use, or in some circumstances used for commercial research and development (R&D) purposes, until sufficient familiarity is gained with their behavior. As EPA acquires familiarity with new microorganisms through reviews or other avenues, EPA expects certain of these organisms to become eligible for reduced reporting or to be eliminated from screening altogether.

EPA recognizes the enormous potential of biotechnology to fight disease, pollution, and hunger, and to replace some chemicals that are harmful to the environment. The realization of these benefits depends upon public confidence in the safety of biotechnology. Public perception will strongly affect the conduct of field tests and the acceptance of commercial applications of

biotechnology (Ref. 1). At the same time, EPA recognizes the importance of retaining the competitive advantage the United States presently maintains in the development and application of biotechnology. Recognizing that regulations can affect competitiveness and public acceptance either negatively or positively (Ref. 2), EPA is proposing rules that it believes balance the needs of the public without adversely affecting the capacity for innovation.

*B. Role of This Proposed Rule in the Federal Coordinated Framework For Regulation of Biotechnology*

This proposed rule implements EPA's program for oversight of microorganisms in accordance with the Federal ''Coordinated Framework for Regulation of Biotechnology; Announcement of Policy and Notice for Public Comment'' which was published by the Office of Science and Technology Policy (OSTP) on June 26, 1986 (51 FR 23302, 23313). EPA's policies regarding use of its statutes to regulate biotechnology products are published in the ''Statement of Policy: Microbial Products Subject to the Federal Insecticide, Fungicide, and Rodenticide Act and Toxic Substances Control Act'' (''1986 Policy Statement'') which was published as part of the Coordinated Framework. EPA is currently operating its biotechnology program under the 1986 Policy Statement.

Prior to the 1986 Policy Statement, EPA issued a ''Proposed Policy Regarding Certain Microbial Products'' on December 31, 1984 (49 FR 50880) (''1984 Proposed Policy Statement''). Subsequent to the 1986 Policy Statement, EPA issued a notice, entitled ''Biotechnology; Request for Comment on Regulatory Approach'' on February 15, 1989 (54 FR 7027), in order to solicit comments on the direction of EPA's program under TSCA. Comments on the 1984 and 1986 documents and the February 15, 1989 Federal Register notice are addressed, as appropriate, in this preamble.

On September 7, 1990, EPA convened a subcommittee of its Biotechnology Science Advisory Committee (Subcommittee on Implementation of Scope) to comment on topics associated with this proposed rule. EPA again convened a subcommittee, the Subcommittee on the Proposed Biotechnology Rule under TSCA, which met on July 22, 1991. Advice from both of these subcommittees has been incorporated as appropriate in this preamble, and summaries of subcommittee deliberations have been placed in the docket for this rulemaking. This proposed rule announced today is intended to describe implementation of EPA's program for regulation of microorganisms under TSCA.

*C. Statutory Framework*

This Unit describes the TSCA provisions used for this rulemaking.

1. *Jurisdiction.* TSCA authorizes EPA to regulate any chemical substance, except for certain substances covered by other Federal agencies. The Act defines chemical substance broadly enough to cover microorganisms. Specifically, section 3(2) of TSCA defines chemical substance, in part, as any organic substance of a particular molecular identity including any combination of such substances resulting in whole or in part from a chemical reaction or occurring in nature.

a. *Organisms are chemical substances.* The TSCA definition of chemical substance describes any deoxyribonucleic acid (DNA) or ribonucleic acid (RNA) molecule, however created, that is a component of an organism's genetic material. Similarly, a microorganism is a chemical substance, because it is a combination of substances of particular identities that occur in nature or occur, in whole or in part, as a result of a chemical reaction (Ref. 3). EPA has consistently applied this definition to life forms and in the 1984 Proposed Policy Statement (49 FR 50886-87) clarified that this interpretation applies to microorganisms. While the statutory term ''chemical substance'' has been interpreted to include microorganisms, EPA acknowledges that microorganisms are not generally referred to as chemicals. Therefore, throughout this preamble, the term ''traditional chemicals'' will be used to refer to chemical substances other than microorganisms.

The fact that microorganisms can be considered chemical substances under TSCA only establishes EPA authority over them. Implementation of that authority requires further action, either to interpret specific terms or to issue rules. Discussion of the types of microorganisms covered in this proposal can be found in Unit IV.A. of this preamble.

b. *Plants and animals are not subject to this proposed rule.* Plants and animals could also be chemical substances under TSCA. Nevertheless, as a matter of policy, EPA has limited this rulemaking to microorganisms, e.g., microalgae of the plant kingdom. Transgenic plants and animals are not subject to requirements under this proposed rule, either as whole organisms or when their cells or parts of cells are cultured in vitro. However, microorganisms into which plant or animal gene segments are intentionally incorporated would be considered microorganisms potentially subject to TSCA. Traditional chemicals extracted from a plant or animal also may be subject to TSCA, as are other chemical substances. EPA is reserving authority under TSCA to screen transgenic plants and animals in the future as needed.

c. *Microorganisms excluded by statute.* The definition of ''chemical substance'' in TSCA excludes pesticides, tobacco and tobacco products, food, food additives, drugs (including human drugs, animal drugs, and animal biologics), cosmetics, and substances that are used as medical devices. These substances are regulated under other statutes by the EPA Office of Pesticide Programs, the United States Department of Agriculture (USDA),

or the Food and Drug Administration (FDA).

Certain microorganisms that are subject to TSCA but are also known plant pests are regulated jointly by EPA under TSCA and the USDA under the Federal Plant Pest Act. In cases where microorganisms are not known to be plant pests, the microorganisms used for TSCA purposes would be regulated solely by EPA. However, USDA would become involved if an EPA review determined that the microorganism had plant pest qualities.

d. *Microorganisms used as intermediates.* Microorganisms may be used as intermediates to produce substances that are in turn used as products subject to TSCA or other statutes. Under the Federal Food, Drug, and Cosmetics Act (FFDCA), intermediates used to make products subject to FFDCA are considered to be components of foods, food additives, drugs, cosmetics and medical devices, as the case may be. Therefore, those microorganism intermediates are excluded from regulation under TSCA. All other intermediates, including pesticide intermediates, are subject to TSCA jurisdiction. Traditional chemicals not excluded from TSCA and produced by microorganism intermediates are subject to TSCA section 5. These chemicals produced by microorganisms are subject to the same requirements and procedures as chemicals produced by other means. EPA discussed its approach to microorganism intermediates and their products in its 1984 Proposed Policy Statement (49 FR 50887, 50890; December 31, 1984).

2. *Application of TSCA section 5.* TSCA gives EPA comprehensive authority to regulate chemical substances and mixtures of chemical substances under four major provisions. Section 4 authorizes the issuance of rules requiring testing of chemicals. Section 6 authorizes the Agency to issue substantive regulations to protect against chemicals that present an unreasonable risk. Section 7 authorizes protection against imminent hazards. EPA has based its biotechnology rulemaking efforts on section 5, the other major TSCA provision. Section 5 establishes a 90-day process for EPA to screen certain chemical substances before they are produced. Within the 90 days following receipt of notification, EPA has to decide whether to drop the substance from further consideration or to impose controls.

Section 5(a) allows EPA to require submission of a notification for two types of microorganisms, those that are considered ''new'' chemical substances and those that will be made for a ''significant new use.'' In both cases, notification is not triggered by a determination that a risk is present. Risk is fully considered during or after the screening process. Those substances defined as ''new chemical substances'' are automatically subject to notice requirements. Chemical substances which are made for a significant new use are subject to notification when EPA issues a rule for the particular substance.

While the statute TSCA does not distinguish between the form or content of the notifications for new substances or new uses, EPA's current regulatory program, which is largely applicable to traditional chemicals, does. The notification for a new chemical substance is called a premanufacture notice (PMN). The notification for a significant new use is called a significant new use notice (SNUN). For the biotechnology program, however, EPA is proposing to refer to either type of notification as a Microbial Commercial Activity Notice or MCAN.

Notices under section 5(a) are submitted by manufacturers of new chemical substances, and by persons who manufacture or process chemical substances for a significant new use. TSCA section 3(7) defines ''manufacture'' to mean import into the United States, production or manufacture. Thus, the word manufacture as used in this preamble refers to importation and any type of production, as well as to those activities that may commonly be considered manufacture. TSCA section 3(10) defines ''process'' as preparation of a substance, after its manufacture, for distribution in commerce.

a. *Distinction between ''commercial purposes'' and ''general commercial use.''* TSCA section 5(i) limits section 5 screening to activities ''for commercial purposes.'' The term ''commercial purposes'' applies to all activities that derive actual or potential commercial benefit for persons associated with those activities. This includes R&D designed to result in a commercial product, whether or not a product is actually developed. A discussion of various options for EPA to decide what constitutes commercial purposes under this rule appears at Unit III.A.

These rules propose different review procedures for microorganisms used for commercial R&D and for microorganisms that are no longer in R&D and are intended for commercial distribution. In order to distinguish between commercial R&D and other types of commercial activity, EPA is describing use for commercial purposes beyond R&D as ''general commercial use.''

b. *Definition of ''new.''* The term, ''new chemical substance,'' is defined at TSCA section 3(9) as a substance not on the TSCA Inventory of Chemical Substances (''Inventory'') manufactured in the United States. Compilation and publication of the Inventory is a requirement imposed on EPA by TSCA section 8(b). When EPA completes review of a new substance, the substance is placed on the Inventory upon EPA's receipt of a Notice of Commencement which indicates that production has begun. At this point, the substance is no longer new, and subsequent producers do not have to submit PMNs.

EPA has a longstanding policy of not explicitly listing on the Inventory unprocessed naturally occurring

substances. Instead, these substances are considered to be implicitly included on the Inventory (see 40 CFR 710.4(b)). Thus, they are not ''new'' and do not require PMNs.

In defining what constitutes an unprocessed naturally occurring substance, EPA has distinguished between substances isolated from nature using more or less mechanical means and those isolated from nature using more sophisticated forms of human intervention, such as chemical reactions. The latter substances remove from a natural product something that, by itself, does not exist in nature. One example is that natural latex extracted from trees is a naturally occurring substance, but the rubber formed after chemical coagulants are added is not (42 FR 64589, December 23, 1977).

EPA is retaining for this rulemaking its interpretation of ''new'' microorganisms as discussed in the 1986 Policy Statement. Under that interpretation, microorganisms resulting from deliberate, intergeneric combinations of genetic material constitute ''new'' microorganisms subject to PMN requirements. For the purposes of the Policy Statement, the Agency defined intergeneric microorganisms as those formed by deliberate combinations of genetic material from source organisms in different genera. EPA may decide to reconsider its interpretation of ''new'' microorganism at a later time and in aseparate rulemaking. EPA requests comment on whether it should explore alternative interpretations of ''new'' microorganism.

In the 1986 Policy Statement, EPA excluded from the definition of a ''new'' microorganism, those microorganisms that have resulted from the addition of intergeneric material that is well-characterized and contains only non-coding regulatory regions such as operators, promoters, origins of replication, terminators, and ribosome-binding regions. EPA is also proposing to retain this exclusion as part of its interpretation of ''new'' microorganism.

In the course of implementing the 1986 Policy Statement, the Agency recognized that it had to develop additional guidance concerning the definition of a new microorganism. It became apparent that a policy was needed to address certain genetic elements which can be transferred between microorganisms of different genera. These are termed mobile genetic elements (MGEs) and include plasmids and transposons. EPA developed additional guidance concerning whether microorganisms modified using vectors that contained MGEs or parts of MGEs were considered new. The Agency indicated that the major consideration is the source of the original isolation of the MGE. EPA stated that microorganisms would be considered ''new'' and thus subject to PMN requirements, if the MGE was originally isolated from a microorganism in a genus different from the recipient genus. Microorganisms would be considered intrageneric, and hence not subject to PMN requirements, if the MGE was originally isolated from a microorganism in the same genus as the recipient.

The Agency has adopted this interpretation for reasons of regulatory clarity and uncertainty about the possibility of the resulting microorganism exhibiting new traits. For example, some MGEs may contain genetic material that normally is not expressed in one microorganism but, when inserted into another microorganism, may be expressed and result in a new trait. Since the Agency plans to continue to use the 1986 Policy Statement interpretation of ''new'' to be intergeneric microorganisms, the Agency will continue to use this MGE guidance to clarify what microorganisms would be subject to TSCA section 5 reporting. EPA specifically requests comments on whether the MGE interpretation provides appropriate assistance for determining whether a microorganism is intergeneric or whether additional modifications which would be useful in clarifying which intergeneric microorganisms should be reported under TSCA section 5.

c. *Significant new use.* EPA determines a use is a significant new use by issuing a rule. The rule is called a significant new use rule or SNUR. Section 5(a)(2) sets forth some of the relevant considerations for issuing a SNUR. The considerations generally include changes in the type or form of exposure to a substance. Although EPA is not proposing any specific SNURs in this rulemaking, EPA is proposing to set up processes for issuing SNURs for microorganisms if needed in the future. See Unit IV.C. of this preamble for a discussion of the proposed SNUR processes.

d. *Section 5 regulatory mechanisms.* If the 90–day period provided for review of a PMN or SNUN expires and EPA has taken no action, production of the substance may begin. However, within the review period, EPA may prevent or limit production of the substance under section 5(e) or 5(f). Under section 5(e) EPA may issue an order prohibiting or limiting production of a substance, if the Agency determines that information is insufficient and the substance may present unreasonable risk or its use may result in substantial exposure. If the notification submitter objects, the section 5(e) order does not take effect and EPA may go to court to obtain an injunction to accomplish the same goals as the section 5(e) order.

Alternatively, if EPA finds that a substance presents or will present an unreasonable risk, the Agency may, under section 5(f), go to court for an order restricting or prohibiting production or issue an administrative order or immediately effective rule to accomplish that result.

If EPA decides subsequent to Inventory listing that further oversight is needed, the Agency may use other provisions of TSCA. These could include SNURs or other rules that would require testing (TSCA

section 4), information submission (TSCA section 8) or substantive restrictions (TSCA section 6).

e. *Exemptions from the section 5 notification process.* Section 5(h) provides for certain exemptions from screening. Three are relevant to biotechnology. Section 5(h)(1) allows manufacturers or processors of substances only for test marketing to apply to EPA for an exemption from full notification. Unit II.C.3. of this preamble discusses the test marketing exemption (TME) for microorganisms.

Section 5(h)(3) provides that the screening mechanisms do not apply to substances manufactured or processed only in ''small quantities'' for R&D, provided that persons engaged in R&D activities for a manufacturer are notified of any risks to health associated with the substance. Section 5(h)(3) authorizes EPA to define by rule what constitutes small quantities and to prescribe the form and manner of risk notification. EPA is proposing a small quantities definition that is limited to contained structure R&D uses of microorganisms. There would be no small quantities exemption for microorganisms introduced into the environment during commercial R&D, thus use of such microorganisms must be reviewed. This modification is described at Unit II.D. of this preamble. The rationale for this modification is discussed at Unit III.B. of this preamble.

Section 5(h)(4) allows EPA to exempt new substances from all or part of section 5 screening requirements, if the Agency determines, by rule, that such substances will not present an unreasonable risk. EPA is proposing to use section 5(h)(4) to exempt certain categories of microorganisms from screening as new microorganisms. Additionally, EPA is proposing under section 5(h)(4) to allow R&D introductions of microorganisms into the environment on the condition that EPA has approved them through expedited review of information submitted in a TSCA Experimental Release Application, or TERA. The TERA process is described in Unit II.D. of this preamble. EPA is also proposing other section 5(h)(4) exemptions for specific microorganisms and classes of microorganisms as described in Unit II.C. of this preamble. The rationale for all exemptions proposed under section 5(h)(4) appears in Unit III.C. of this preamble.

3. *Substantial risk notification.* Section 8(e) requires reporting by manufacturers, processors and distributors who come across information that their chemical substance could cause a ''substantial risk.'' Section 8(e) is a self-implementing provision of TSCA. Thus, if a manufacturer, processor or distributor of a microorganism finds applicable information, that information must be submitted to EPA. Unit IV.F. of this preamble discusses section 8(e) in further detail.

4. *Applicability of TSCA section 26.* Section 26(c) authorizes EPA to take any action under TSCA for a category of chemical substances. EPA proposes to use this authority extensively in this rule. The reasons for grouping microorganisms into categories, which include new microorganisms used for R&D and certain new microorganisms manufactured for general commercial use, are explained in applicable sections.

## II. Structure of the Proposed Rule

This portion of the preamble discusses the major provisions of these rules. The rationale supporting these provisions follows in Unit III. Unit II.A. describes how to determine whether reporting is required. Unit II.B. describes general administrative procedures that would be applicable to all notices submitted. To facilitate understanding of this proposed rule, requirements for microorganisms manufactured for general commercial use are discussed separately from those for microorganisms used for commercial R&D. Unit II.C. describes procedures applicable to microorganisms which are manufactured for general commercial use. Unit II.D. contains a similar description of procedures applicable to microorganisms used for R&D.

While these regulations are modelled after and incorporate many of the procedures in the existing TSCA section 5 screening program for traditional chemical substances which EPA has operated for the past decade, modifications have been made, as appropriate, to address the specific characteristics of microorganisms. In this respect, this proposed rule incorporates well-established procedures which EPA has adopted in previous rulemakings. The procedures are currently contained in the Code of Federal Regulations (''CFR'') at parts 720 (premanufacture notification) and 721 (significant new use notification requirements). EPA has decided, however, to establish a new part in the CFR which applies specifically to microorganisms. EPA believes that placing regulations affecting microorganisms screened under TSCA section 5 in one place, part 725, will be more convenient and efficient.

EPA has only made changes to the procedures in parts 720 and 721 to the extent required by unique characteristics of microorganisms. EPA is therefore not soliciting comment on the procedures in proposed part 725 that are incorporated from parts 720 and 721.

EPA will only consider comments to the extent they address the new procedures and requirements in proposed part 725.

In addition to a preferred approach for certain issues, this preamble often contains a discussion of alternatives. EPA solicits public comment on the preferred approaches and the alternatives discussed in this document. Depending on public comment received on the various proposals, any of these alternatives may be adopted in the final rules.

### *A. Determining Whether Reporting Is Required*

Manufacturers or processors would follow the process laid out below to

determine whether their microorganism is subject to reporting and, if it is, how it would be treated under this proposed rulemaking. They must first determine whether their microbial products are subject to TSCA. Subpart A of part 725 contains the regulations applicable to this determination. Many microorganisms are not subject to the requirements of this proposed rule, because they are statutorily outside the jurisdiction of TSCA. Statutory jurisdiction is discussed in Unit I.C. of this preamble.

1. *Determining whether a microorganism is new or subject to a SNUR*. After manufacturers of microorganisms determine that their products are subject to TSCA, they must determine whether the microorganisms are new. Section 725.3 defines a new microorganism as one that is not included on the Inventory. Microorganisms may be either implicitly or explicitly included on the Inventory.

a. *Implicit inclusion*. In its 1986 Policy Statement, EPA stated that intergeneric microorganisms were the only microorganisms that would not be implicitly included on the Inventory. As discussed in Unit I.C. of this preamble, EPA will continue to use the 1986 Policy Statement interpretation for this rulemaking.

b. *Explicit listing*. A microorganism is not new, if it is explicitly listed or implicitly included on the Inventory. Microorganisms are placed on the Inventory if they have been previously manufactured in the United States for general commercial use. EPA explicitly lists microorganisms that it has previously reviewed, after it is informed that production has begun through receipt of a Notice of Commencement of Manufacture (NOC) (see § 725.190). If a microorganism is not considered to be implicitly included on the Inventory, the public Inventory needs to be consulted to determine whether the microorganism is explicitly listed. Microorganisms may also be explicitly listed but treated as confidential and not placed on the public Inventory.

c. *SNUR listing*. After persons determine that their microorganisms are included on the Inventory, they must then check to see if the microorganisms are subject to a SNUR. Where appropriate, microorganisms subject to SNURs will be identified, both on the Inventory and in Subpart M of part 725. The SNUR process is discussed in Unit IV.C. of this preamble.

2. *Consulting EPA when microorganism identity or use is confidential or uncertain*. Specific situations arise under these rules when persons would need to consult listings of microorganisms to determine whether a particular microorganism, or use of a microorganism, is subject to reporting. These listings include the Inventory; Subpart M of part 725, which lists significant new use rules; and § 725.239, which lists certain microorganisms exempt from R&D reporting under part 725. The listings are explained in the text of the regulation.

There would be two specific circumstances under which it may not be possible to determine whether a particular microorganism is listed. First, the actual identity or use may be claimed confidential by a person who originally manufactured or processed the microorganism. In this case, a so-called generic name or use would appear on the public Inventory, and the actual identity or use would be on a confidential listing not available to the public. Unit IV.D. on Confidential Business Information (CBI) explains the generic name and use. The second circumstance would be that a non-confidential identity of a microorganism may not be precise enough for a person to determine whether it describes a particular microorganism that could be subject to reporting. This circumstance may arise because of the imprecision of scientific nomenclature in biology, particularly in microbiology, or because similarities in modified genetic material may raise questions of equivalency (see Unit IV.B.).

To assist persons in determining their reporting obligations, EPA has established a procedure whereby a person may file a submission establishing a *bona fide* intent to manufacture or process a microorganism and request that the Agency determine whether that microorganism is on the applicable listing. EPA's goal is to respond in 30 days to the request, informing the requestor whether there is an obligation to report under these regulations (see § 725.15). This procedure allows EPA to ensure appropriate reporting while maintaining the confidentiality of legitimate trade secrets. This is a well-established procedure in the Agency's current regulations on TSCA section 5 reporting (see §§ 720.25 and 721.11). This preamble will note when this process, known as a ''*bona fide*,'' applies.

### *B. General Administrative Procedures*

After submitters determine that they have a microorganism subject to TSCA section 5, they must determine what type of submission will satisfy their reporting obligations. The first decision is whether the microorganism will be used for R&D or general commercial use. The specifics of the submission and review processes for general commercial use and for R&D are covered in Units II.C. and II.D. of this preamble, respectively. However, some administrative procedures apply generally to all microorganism submissions. Therefore, general administrative procedures are discussed in this Unit.

Subpart B of part 725 contains administrative procedures generally applicable to all submissions. Most of these are rather mechanical, such as general recordkeeping requirements, procedures for determining whether submissions are complete and properly filed, how to determine when the Agency will begin the review period designated for a particular submission, and

under what circumstances the Agency or the submitter may suspend, extend, or terminate a review. The more important administrative procedures are discussed in this Unit.

1. *Prenotice consultation*. EPA recommends that potential submitters begin discussions with EPA staff early in the submission planning process to identify any special data requests and preliminary concerns that may be associated with the microorganism. This may save significant time later in the review process. Any meetings and relevant written communications may be claimed confidential. Persons who are unsure as to whether their microorganisms are subject to any of the requirements of part 725 should consult with EPA before preparing any submission.

With reference to R&D, EPA recognizes that research proceeds through various stages. Potential submitters may find it advantageous to begin discussions with EPA as early as the grant proposal stage, even though they would not be required to file a submission under part 725 until the latter stages of their research program. Early consultation with the Agency could assist submitters in the planning stages of their research program in addition to providing a smoother submission and review process.

2. *Submission process*. The general requirements pertaining to the submission process are found at §§ 725.25 through 725.36.

a. *Preparing submissions*. The data to be included in submissions for microorganisms would be different from those for traditional chemicals, because microorganisms may pose different risks than those posed by traditional chemicals. To assist persons preparing submissions under this proposed rule, EPA has developed a special guidance document entitled ''Points to Consider in the Preparation and Submission of TSCA Notifications for Microorganisms.'' At this time, a special form has not been developed for microorganism submissions. Therefore, persons preparing microorganism submissions should follow the format outlined in the guidance document. This document is available from the Environmental Assistance Division (see the address listed under the FOR FURTHER INFORMATION CONTACT Unit).

The regulatory text describes the type of information that is relevant for each specific type of submission. Submitters should submit all reasonably ascertainable information which they believe will assist EPA in evaluating the microorganisms, including information not specifically listed that submitters believe will be useful for EPA's risk assessment. When information listed in the regulatory text is not submitted, a brief explanation of why such information is not available or not applicable should be included. Prenotice consultation may assist in identifying specific information appropriate for a submission.

b. *Incomplete submissions*. After an initial evaluation, EPA may determine that a submission is incomplete and that the review period cannot begin (see § 725.33 of the regulatory text). If EPA finds the submission incomplete, EPA will notify the submitter within 30 days of receipt of the submission and will provide the submitter with an opportunity to provide additional information. If the submitter promptly provides additional information sufficient to evaluate the effects of the microorganism, the evaluation will not be delayed beyond time for a reasonable consideration of the new information. Otherwise, EPA may declare the submission incomplete and the review period will not begin until EPA receives the necessary information.

3. *Review process*. The requirements pertaining generally to the review process are found at proposed §§ 725.40 through 725.60.

a. *Public involvement*. EPA is aware that there is considerable public interest in the review of submissions involving new microorganisms and is committed to keeping the process as open as possible. Following receipt of a submission, EPA is required by TSCA to issue a notice in the **Federal Register** describing the submission (see § 725.40 of the regulatory text). The **Federal Register** notice would include nonconfidential information on such items as the identity of the microorganism, the type of use, occupational exposure, production volume, a summary of test data included in the submission, and the submitter's identity. If microorganism identity and use are claimed confidential, EPA includes generic descriptions of this information in the Federal Register notice. Unit IV.D. of this preamble discusses confidentiality and generic descriptions. EPA would maintain a nonconfidential copy of the submission in the TSCA Nonconfidential Information Center for public inspection. The public will have an opportunity to comment on submissions received by EPA. The length of the comment period may be affected by the need to hold a meeting of experts to address a particular submission, or to consider novel scientific issues raised by the submission.

b. *State coordination*. EPA has developed comprehensive procedures to coordinate reviews of submissions and to share scientific information to the fullest extent with appropriate State and local authorities. For example, under EPA's current procedures for review of field tests under the 1986 Policy Statement, within the first week of receipt of a submission, an EPA review coordinator contacts by telephone the appropriate regulatory agencies in the State(s) where the test will be conducted to inform them of the submission. If requested, a nonconfidential copy of the submission is mailed to the State. If a site visit is to be conducted, EPA staff contacts State and EPA regional personnel early in the review period to begin coordination of the site visit. Nonconfidential reports, assessments,

and public comments added to the Public Docket are routinely made available to State personnel upon request. In addition, State personnel receive a copy of EPA's draft risk assessment, and comments and concerns raised by the State(s) are given careful attention in the risk assessment. At the conclusion of the review period, State personnel receive a copy of any document which addresses the conditions under which the field test can be performed.

EPA is also requiring that persons who are preparing submissions for R&D activities provide evidence of having notified appropriate State authorities (see § 725.255 of the regulatory text). Submission of copies of any correspondence with State authorities concerning the proposed field trial, for example, would satisfy this requirement. EPA also strongly encourages such submitters to inform communities located near potential test sites of their plans to introduce microorganisms into the environment.

c. *Use of experts*. In performing assessments, EPA intends to supplement its staff expertise as necessary by using experts from other government agencies, academia, and other independent sources. EPA assessments may be reviewed by a subcommittee, composed of scientists with relevant expertise, of EPA's Biotechnology Science Advisory Committee (BSAC) at a public meeting. Certain portions of the meetings may be closed to discuss confidential business information (CBI). EPA will consider all BSAC Subcommittee recommendations in its final decisions. Procedures have been developed to ensure that experts contributing to EPA's biotechnology reviews will not have conflicts of interest.

d. *Changes to the review process*. The review period starts on the date EPA determines the submission is complete and runs for a period of time specified for each submission type. A submitter may voluntarily withdraw a submission at any time, or suspend the review period for a specified period of time. Suspension of the review period may be beneficial when questions that arise during the notice review period require additional time to address. For good cause, EPA may extend the review period up to a total of the length of time specified for each type of submission.

4. *Recordkeeping and compliance*. The requirements for recordkeeping, compliance, and inspections are found at §§ 725.65, 725.70, and 725.75, respectively. In addition to recordkeeping requirements generally applicable to all submissions, EPA is proposing recordkeeping requirements specific to each submission type. For certain exemptions from full reporting under section 5, the recordkeeping requirements are a key part of compliance with the exemption. Compliance and inspection requirements are the same as those for traditional chemicals.

5. *Petitions to exempt new microorganisms*. Provisions for applications to request exemptions for new microorganisms from the requirements of all or part of part 725 are found at § 725.67.

### *C. Reporting General Commercial Use of TSCA Microorganisms*

This Unit discusses who is subject to microbial commercial activity notice (MCAN) reporting, the MCAN submission and review process, and exemptions from MCAN reporting for general commercial use.

1. *Determining whether MCAN reporting is required*. Subpart D of part 725 would require, with some exceptions, submission of a MCAN by persons who intend to manufacture or import new microorganisms, and by persons who intend to manufacture, import, or process microorganisms for a significant new use. A MCAN must be submitted 90 days before manufacture, import, or processing of the microorganism for commercial purposes. Because EPA has a separate, less burdensome, screening process for R&D involving microorganisms (see Unit II.D. of this preamble), the Agency expects that, in general, the MCAN will be submitted only for microorganisms for general commercial use.

2. *MCAN submission and review process*—a. *MCAN submission process*. The purpose of EPA's review of MCANs would be similar to EPA's purpose in reviewing PMNs and SNUNs submitted for traditional chemical substances. The purpose of a MCAN would be to provide EPA with information necessary to identify and list a microorganism on the TSCA Inventory (if the microorganism is new) and to determine whether the microorganism would pose an unreasonable risk to human health or the environment. EPA must conduct a review that considers all the reasonably ascertainable information on potential human health and environmental effects of a microorganism. The information to be included in the MCAN is listed in §§ 725.155 and 725.160 of subpart D. Submitters must develop a MCAN that describes the characteristics and construction of the new microorganism as well as describing conditions of manufacture and use. In addition, submitters must reference any published literature on the microorganism and its parental strains and submit available data from laboratory, greenhouse studies, and/or R&D field tests using the microorganism.

b. *MCAN review process*. All reviews of microorganisms will follow established administrative steps that are the same for all chemical substances subject to 90-day review. For good cause, EPA may extend the initial review period by an additional 90 days, for a total of 180 days. During this time the microorganism cannot be manufactured or processed for commercial purposes.

c. *Regulatory decision*. EPA may reach one of three decisions during

the review period based on a balancing of the risks and benefits presented by the microorganism: There is sufficient information to determine that the risks will not be unreasonable; there is sufficient information to determine that the risks are unreasonable; or there is insufficient information to make a reasoned evaluation of risk, and the substance may present an unreasonable risk or there may be significant or substantial human or environmental exposure to it.

Unless EPA notifies the submitter to the contrary, the submitter may begin to manufacture and use the microorganism at the end of the 90–day period. However, if the information available is insufficient to reasonably evaluate the risk and the substance may present an unreasonable risk, EPA may issue an order under TSCA section 5(e) to limit or prohibit the manufacture, processing, distribution in commerce, use, or disposal of the microorganism. In the past, EPA has found it useful to negotiate with submitters to develop consent orders, sparing both the submitter and EPA the legal proceedings that may be involved in a unilaterally issued order. Under a consent order, the submitter generally agrees to develop additional information or to accept certain restrictions in return for permission to proceed with its plans to manufacture or import the substance.

In the situation where EPA decides that risks will be unreasonable, it may use TSCA section 5(f) to require measures to reduce risks to an acceptable level as a condition of manufacture and use. Alternatively, EPA may prohibit manufacture or use, if there are no measures available or practicable to sufficiently reduce the risk.

3. *Exemptions from MCAN reporting*. Persons intending to manufacture new microorganisms for general commercial use may not have to submit a MCAN prior to commencing manufacture, if the microorganisms they intend to use qualify for exemptions from MCAN reporting. This unit discusses one exemption developed for traditional chemicals that will not be applied to microorganisms and two exemptions that are applicable to microorganisms.

a. *Low volume exemption*. EPA has previously promulgated rules providing for an exemption from the notification requirements of section 5 of TSCA for new chemical substances produced for general commercial use in volumes less than 1,000 kilograms per year (see 40 CFR 723.50). This exemption requires applicants to submit a notice to EPA 21 days before manufacture begins to provide the Agency an opportunity to review the chemical. EPA believes that this exemption is inappropriate for microorganisms, which have the ability to reproduce, disseminate, and transfer genetic material. EPA is therefore proposing to amend § 723.50 to state that the exemption provisions of that section do not apply to microorganisms.

b. *Test marketing exemption*. Test marketing activities usually involve limited sale or distribution of a substance within a predetermined period of time to determine its competitive value when its market is uncertain. EPA is required by TSCA section 5(h)(6) to grant or deny the test marketing exemption (TME) no later than 45 days after receipt of an application. Subpart F of part 725 proposes the requirements for obtaining a TME. These requirements are adopted verbatim from § 720.38, the Agency regulations that currently apply to all chemicals substances.

In general, EPA suggests that manufacturers who intend to test market new microorganisms file a MCAN rather than a request for a TME. However, there may be situations in which this exemption may be appropriate, such as for microorganisms which were previously reviewed by EPA at the R&D stage. EPA encourages anyone who is considering requesting a TME for a new microorganism to begin prenotice consultation as early as possible, so that EPA can determine if it would have sufficient information to determine that the test marketing activities would not present an unreasonable risk.

c. *Tiered exemption for general commercial use*. Under TSCA section 5(h)(4), EPA is proposing to exempt from MCAN requirements certain new microorganisms manufactured for general commercial use which it has determined will not present an unreasonable risk. Subpart G of part 725 contains the conditions for this exemption, which consists of two tiers, each based on certain criteria discussed below. The rationale for this exemption appears in Unit III.C.7. of this preamble. Microorganisms produced under this exemption would not be listed on the Inventory.

(i) *Tier I*. Manufacturers meeting Tier I requirements will be completely exempt from review by EPA. They would submit a one-time certification statement to EPA 30 days prior to the first use of a microorganism eligible for a Tier I exemption. The conditions for this exemption are listed at § 725.424. The statement must include information identifying the manufacturer or importer, the location of the facility involved, and a statement certifying that the manufacturer complies with all the criteria required for the Tier I exemption. Information in the statement may be claimed confidential. A certification would be required for the first use of an eligible recipient microorganism at a specific facility. Subsequent uses of the same recipient microorganism at the same facility would not require additional certification, so long as the manufacturer complied with the other Tier I exemption conditions.

(ii) *Tier II*. Manufacturers meeting the requirements at proposed § 725.428 may submit an exemption request to EPA 45 days prior to use of the microorganisms, if they believe that containment conditions other than those listed at proposed

§ 725.422 would still allow the requirements of the exemption to be met (see § 725.455 of the regulatory text). Information included in such a submission may be claimed confidential. Submitters must certify in the request that they have complied with the requirements. EPA would approve or deny an exemption request within 45 days and could impose restrictions to ensure that the microorganisms would not present an unreasonable risk (see § 725.470 of the regulatory text).

(iii) *Criteria for the exemption*. Three conditions are placed on the Tier I and Tier II exemptions. The recipient microorganisms must be listed at proposed § 725.420, the introduced genetic material must meet certain requirements, and performance-based criteria for containment and inactivation of the new microorganisms are to be used.

(A) *Recipient microorganisms*. EPA is proposing that new microorganisms certified to be developed using a recipient species or strain listed at proposed § 725.420 would qualify for the tiered exemption.

(B) *Introduced genetic material*. The introduced genetic material used to modify the recipient microorganisms must be well characterized, limited in size to the genetic material required to perform the intended function, and poorly mobilizable (see § 725.421 of the regulatory text). Further explanation of these terms appears in Unit III.C.7. of this preamble. In addition, genetic material which encodes for all or part of the toxins listed in proposed § 725.421(d) may not be used to modify any recipient microorganism.

(C) *Containment and inactivation*. EPA is also proposing performance-based criteria for limiting exposures. These criteria would have to be used for the Tier I exemption, because EPA would not review these activities prior to production. For the Tier II exemption, because the containment and inactivation controls would be reviewed in the exemption request, the criteria would serve as guidance for submitters. Proposed § 725.422 lists the criteria for containment and inactivation at a facility.

(iv) *Exemption applications*. Using the provisions in proposed § 725.67, individuals may submit an application under section 5(h)(4) requesting that a recipient microorganism be added to the exempt list. Submitters may request an exemption with different conditions. EPA would evaluate the request using appropriate procedures under section 5(h)(4).

*D. Reporting R&D Activities for TSCA Microorganisms*

This Unit discusses EPA's proposal for which microorganisms are subject to R&D reporting and recordkeeping, exemptions from R&D reporting, and the TSCA experimental release application (TERA) submission and review process.

1. *Overview of considerations for determining whether a researcher has TSCA section 5 obligations for R&D activities*. Persons planning to conduct R&D activities involving new microorganisms subject to TSCA may be subject to these rules. While any researcher may submit a complete MCAN as required for general commercial use, EPA is proposing a number of exemptions from MCAN reporting that reduce researchers' reporting obligations under TSCA section 5. All R&D activities are eligible for reporting using the TERA process which is discussed below. However, EPA expects that the TERA will be used primarily for environmental experiments. Laboratory and other research in contained structures would more likely comply with certain recordkeeping requirements provided under TSCA section 5(h)(3) in the rule. Finally, certain research may be exempt from TSCA section 5, because EPA has determined review is unnecessary altogether or it is appropriate to defer in whole, or in part, to another Federal agency.

The series of considerations to be used to determine TSCA section 5 obligations for R&D activities is displayed in chart form in Figure 1 below. The following paragraphs summarize the steps on Figure 1.

The first three steps list the issues that must be addressed for determining if any substance is subject to TSCA section 5 reporting, whether for general commercial use or for R&D activities. The subsequent steps are employed to determine R&D obligations. Determining whether an R&D activity is subject to TSCA jurisdiction and whether the microorganism is intended for commercial purposes are discussed below in Units II.D.2.a. and 2.b., respectively. Determining whether a microorganism is ''new'' for the purposes of TSCA section 5 is discussed in Unit I.C. of this preamble.

If researchers have determined that their R&D activities are subject to TSCA jurisdiction, are intended for commercial purposes, and involve new microorganisms, their R&D activities will be subject to some obligations under TSCA section 5. Researchers would then proceed through the remainder of the questions to determine their reporting status. They would first determine whether their R&D activities are eligible for the contained structures exemption. This determination is discussed below in Unit II.D.2.c.

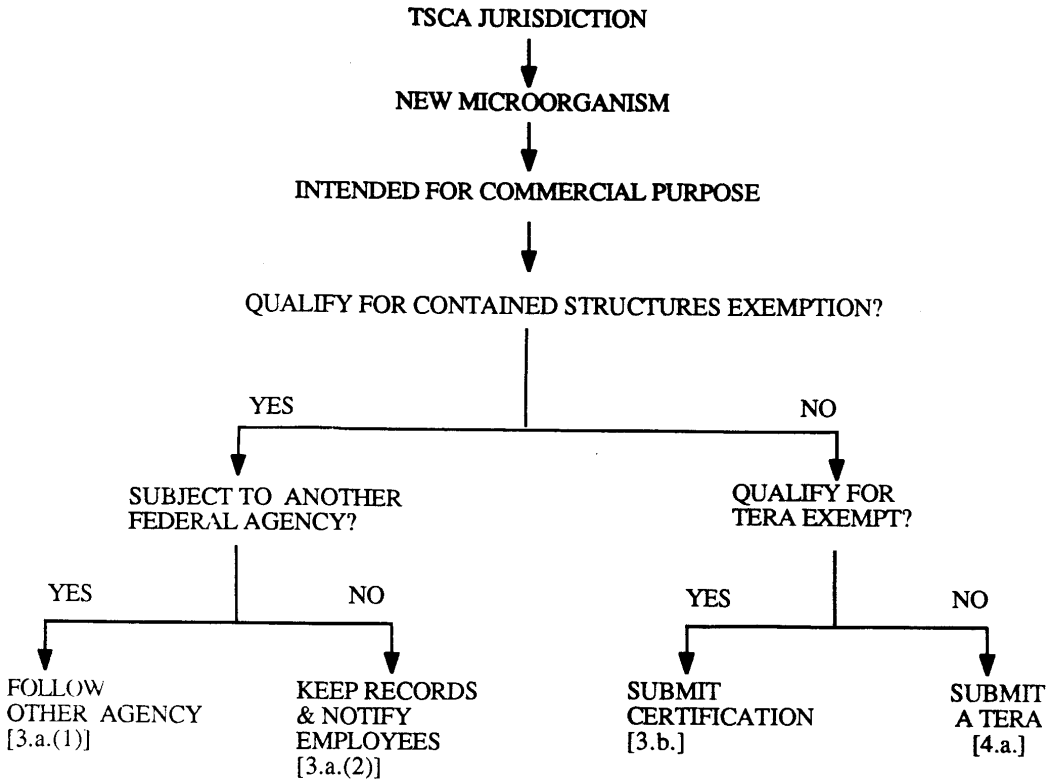
The next question deals with other agencies. An R&D activity that is eligible for the contained structures exemption may also be subject to the authority of another Federal agency. Overlapping jurisdiction for R&D conducted in contained structures is discussed below in Unit II.D.2.d.

If the R&D activity does not qualify for the contained structures exemption, TERA reporting would next need to be considered. However, EPA is also proposing in this rulemaking a category of specific microorganisms that are exempt from TERA reporting. Thus, researchers who are not eligible for the contained structures exemption and/or for deferral to another agency may qualify for a specific TERA

exemption. The determination of whether the research qualifies for a TERA exemption is discussed below in Unit II.D.2.e.

Figure 1 shows the four distinct types of TSCA section 5 obligations existing for R&D activities. The reporting requirements for each of these obligations are discussed below in Units II.D.3. and 4. The corresponding paragraphs are noted on the following Figure 1.

**DETERMINING TSCA SECTION 5 OBLIGATIONS FOR R&D ACTIVITIES**




2. *Specifics for determining eligibility for R&D exemptions*. The five points which researchers must consider in order to determine their TSCA section 5 obligations for R&D are discussed in this paragraph.

a. *Determination that the R&D activity is subject to TSCA jurisdiction*. Statutory jurisdiction is discussed in Unit I.C. of this preamble. As noted in that Unit, uses of some microorganisms are specifically excluded from TSCA section 5, because they are subject to other statutes. Uses that are not specifically excluded are subject to TSCA. When developing the initial TSCA Inventory, EPA indicated that undifferentiated uses of chemical substances would be subject to TSCA (42 FR 64585, December 23, 1977). In the 1986 Policy Statement, EPA stated that unless the uses were explicitly excluded by TSCA, ''all microorganisms produced for environmental, industrial, or consumer uses are potentially regulable under TSCA'' (51 FR 23324, June 26, 1986). Thus, EPA would consider that R&D activities involving new microorganisms where researchers are unsure of the final use would be subject to TSCA section 5. This would include microorganisms in early stages of research, where the researchers have not determined a specific commercial application of the microorganism. As noted in Unit II.B. of this preamble, researchers who are uncertain of the status of their microorganism, for any reason, should consult EPA regarding their TSCA section 5 obligations.

b. *Determination that the R&D activity is intended for commercial purposes*. TSCA section 5 covers only uses of new microorganisms for commercial purposes. EPA discusses its interpretation of commercial R&D in Unit III.A. of this preamble. The Agency is proposing three alternative interpretations of commercial purposes. Depending on public reaction to the alternative interpretations discussed in this proposal, the interpretation of commercial R&D could differ from

one R&D activity to another in a final rule, if public comment supports different interpretations for different types of R&D activities.

c. *Determination that the R&D activity is eligible for the contained structures exemption*. This exemption would most likely apply to research performed in contained structures such as pilot fermentation plants, greenhouses, laboratories, and certain bioreactors used for waste treatment. The term ''structure'' is defined in proposed § 725.3. Research involving intentional testing of microorganisms in the environment would not be eligible for this exemption. Requirements for the exemption are in section 3 of this Unit. The rationale for this exemption is discussed in Unit III.B. of this preamble.

d. *Determination that oversight of the R&D activity is also subject to the authority of another Federal agency*. Some R&D activities may be subject to the authority of another Federal agency in addition to EPA. Where there is overlapping jurisdiction for R&D activities that are eligible for the contained structures exemption, EPA proposes to defer to the other Federal agency which has authority for oversight over such activities. This would apply to researchers who are receiving funding from the other Federal agency, which requires that researchers comply with the ''NIH Guidelines for Research Involving Recombinant DNA Molecules'' (''NIH Guidelines'') in order to receive funding. Researchers who are voluntarily complying with the NIH Guidelines but are not actually receiving funding from a Federal agency would not be eligible for the deferral.

e. *Determination that specific microorganisms are exempt from TERA reporting*. EPA is proposing exemptions from TERA reporting for certain new microorganisms derived from the microorganisms *Bradyrhizobium japonicum* and *Rhizobium meliloti*. R&D involving these microorganisms performed in accordance with specified conditions would be exempt from review. Additional microorganisms may be exempted by rule under section 5(h)(4), as EPA gains familiarity with them. Unit III.C.5. of this preamble discusses the rationale for this exemption.

3. *Requirements necessary for eligibility for exemptions from TERA reporting*. Once researchers have determined which exemptions their R&D activities are eligible for, they must determine their specific TSCA section 5 obligations. Proposed §§ 725.232 through 725.239 specify the requirements for each of the exemptions from TERA reporting.

a. *The contained structures exemption*—(i) *R&D subject to another Federal agency*. R&D activities which are eligible for the contained structures exemption (see § 725.234(a) and (c) of the regulatory text) but are also subject to the oversight of another Federal agency will be exempt from the requirements of TSCA section 5. If researchers comply with the other agency's requirements, there will be no EPA-specific requirements (see § 725.232 of the regulatory text).

(ii) *R&D not subject to another Federal agency*. This document proposes that R&D eligible for the contained structures exemption but not subject to another Federal agency must be conducted in accordance with proposed §§ 725.234 (containment and recordkeeping) and 725.235 (employee notification). Although researchers that comply with these provisions are not required to report to EPA under TSCA section 5, the recordkeeping and employee notification requirements would apply and would be enforceable by EPA.

There are two types of standards in §§ 725.234 and 725.235. The employee notification standards of § 725.235 are taken directly from current regulations in §§ 720.36 and 721.47, and are the same as those for traditional chemical substances. Section 725.234 contains general research standards but adds some provisions that apply specifically to microorganisms. However, these additional provisions are minor changes to EPA's current requirements for the research exemption, and these provisions should be standard practices for research activities involving microorganisms.

Specifically, the small quantities exemption for traditional chemical substances requires research to be conducted by, or directly under the supervision of, a technically qualified individual (TQI). This is a requirement under EPA's current regulations at §§ 720.36 and 721.47. Section 725.234 applies the same requirement to microorganisms eligible for the contained structures exemption.

Section 725.234 states that the TQI must select appropriate measures to control release of the research microorganism, write a brief description of the reasons for choosing the measures and ensure maintenance of records to document routine use of the selected controls. In addition, the choice of control measures must be certified by an authorized official of the institution at which the research is conducted. Finally, EPA may request that the records be sent to EPA for review. Subsequent to such review, EPA may in some circumstances offer recommendations to modify control or documentation measures. In what EPA anticipates would be rare occurrences, EPA might order the researcher to modify controls or documentation measures. Failure to comply with such an order would result in loss of eligibility for the exemption for the specific R&D activity.

For those researchers who are voluntarily complying with, but are not subject to, the NIH Guidelines, the requirements of the contained structures exemption could be met by having the principal investigators serve as the TQIs (see § 725.234(b) of the regulatory text) and keep records indicating that they abide by the NIH Guidelines.

b. *Exemption from TERA reporting for specific microorganisms*. In order

to be exempt from both TERA reporting and MCAN reporting, persons using the exemptions for microorganisms listed in § 725.239 must comply with the general requirements for the exemption listed in § 725.238 as well as any specific requirements listed in § 725.239. Similar to its proposal for the tiered exemption for general commercial use discussed in Unit II.C., EPA is proposing to place restrictions on the recipient microorganisms, the introduced genetic material, and the conditions of use (see § 725.239 of the regulatory text).

4. *TERA submission and review process*. EPA is proposing to establish the TERA, which is an abbreviated notification process for environmental testing of new microorganisms.

*a. TERA submission process*. Sections 725.255 and 725.260 detail specific information that should be submitted with a TERA. The basic microorganism identity information is the same as that for the MCAN. Other information requested specifically addresses the proposed R&D activity and therefore is not as extensive as the MCAN information.

b. *TERA review process*. EPA's goal is to review TERAs in 60 days (see § 725.270 of the regulatory text). For good cause, EPA could extend the initial TERA review period by an additional 60 days, for a total of 120 days (see § 725.56 of the regulatory text). Due to the small number of experiments that have been conducted and the uncertainty concerning field tests that involve new microorganisms, EPA expects that initial TERA reviews may take closer to 120 days. During the prenotice consultation, EPA would estimate for the submitter whether the review is likely to require closer to 120 days or 60 days.

Generally, EPA believes that approval of TERAs in 60 days or less would be possible for field tests that are similar to previously reviewed field tests (for example, use of the same or similar microorganisms, modifications to a previous test, or change in geographic conditions). When novel circumstances are presented in a TERA, however, EPA may need to extend the review period in order to complete its review. Specific examples of extension for good cause would include the need for a subcommittee meeting of the Biotechnology Science Advisory Committee to supplement Agency expertise or the need to coordinate review with other Federal agencies. When EPA coordinates the review of a microorganism with another Federal agency, the review period would automatically be extended to the length of the other agency's review, to allow the two agencies to coordinate reviews and decisionmaking. TERA submitters may not proceed with their field trials until EPA has provided written approval of the TERA submission. As soon as EPA completes its review, however, researchers will be able to start their test immediately upon notification from EPA.

c. *Regulatory decision*. EPA will approve a TERA if it determines that the experiment(s) will not present an unreasonable risk to human health or the environment. If the submission is approved, EPA may negotiate with the submitter a TERA Agreement, which would be legally binding on all parties and would set out any conditions governing the conduct of the specific field trial (see § 725.270 of the regulatory text). The TERA Agreement could include provisions for maintaining restrictions on the use of the test site after the completion of the test. This may require the submitter to make appropriate arrangements with the owner of the test site, in cases where the submitter does not own the test site. If EPA concludes that the proposed R&D activity may present an unreasonable risk of injury to human health or the environment, EPA will deny the TERA and will provide reasons for the denial in writing. Section 725.288 provides for revocation or modification of TERA approvals following the receipt of additional information.

5. *Options for oversight of R&D activities*—a. *Range of options possible*. EPA's intent in offering a variety of alternatives for oversight of R&D activities was to provide a flexible process which tailored oversight to the level of risk. In developing TSCA section 5 obligations for R&D activities using new microorganisms, EPA looked at a range of options. These fall on a continuum ranging from an option which would exempt all R&D activities under a small quantities exemption similar to the exemption for traditional chemicals to an option which would require TERA reporting for all R&D activities, including those conducted in laboratories and other contained structures.

As discussed in Unit III.B. of this preamble, because microorganisms can multiply and spread beyond the site of introduction, EPA must redefine the small quantities definition applied to traditional chemicals. EPA developed the TERA process, because it believes that review of environmental uses of microorganisms should begin during the R&D stage. At the same time, EPA does not believe that all microorganisms used in all R&D activities should be subject to TERA reporting. Neither of the extreme options seemed appropriate to EPA for coverage of R&D, because they would not be tailored to potential risk. Thus, EPA chose an intermediate approach.

In keeping with the goals of the Coordinated Framework, EPA has included in its proposed option opportunities to address overlapping jurisdiction with other Federal agencies. EPA has attempted to balance the Coordinated Framework's goal to reduce duplicative oversight with TSCA section 5's goal to screen for potential unreasonable risks. As discussed in Unit III.B. of this preamble, in developing its requirements for the contained structures exemption, EPA selected an approach which recognized the diversity of microorganisms which

would be used in research and therefore left to the researcher the choice of appropriate containment and inactivation controls. Additionally, in order to keep the TERA process flexible, EPA has developed a provision allowing microorganisms tested in the environment to be exempted from TERA reporting as the Agency gains more familiarity with them.

EPA requests comments on its proposed option for R&D activities for TSCA microorganisms. In particular, EPA would like to know whether commenters feel that the flexibility provided by the various exemptions available under the proposed option counterbalances the complexity of the approach. The public may suggest other options along the continuum, providing those options also meet the intent of TSCA and adequately protect public health and the environment from unreasonable risks. In addition to the proposed option, when EPA prepares its final rule, it will consider the variety of options along the continuum discussed above, as well as options suggested by the public.

b. *Specific alternative for low risk field tests*. EPA realizes that there are a variety of possible options along the continuum discussed above. Although EPA has decided that case-by-case review is important for many microorganisms intentionally tested in the environment, EPA recognizes that there will be low risk field tests that would not require TERA review. For this reason, some have suggested an alternative exemption for certain R&D releases. This alternative, which is similar to the R&D contained structures exemption in that it would be dependent on determinations made by a TQI, would apply to certain low risk field tests and would be included with the exemptions which are part of the proposal for coverage of R&D activities under TSCA section 5. Like the proposed exemption for R&D in contained structures, this alternative would contain requirements for documentation and recordkeeping by a TQI and certification by an authorized company official. It would also provide for EPA to inspect records and order changes, if necessary.

Under this alternative, a company planning a small-scale field test which meets the eligibility requirements for the exemption would have the option of submitting a TERA for review by EPA or submitting a notice with the determination that the field test qualified for the exemption. The alternative includes a number of requirements which are intended to minimize the likelihood of inconsistent determinations.

The TQI would be expected to make the determination that the new microorganism was eligible for the exemption, based on the following: (1) The test site must be 10 acres or less of land, (2) the parent microorganism(s) must have a history of safe use, and (3) the introduced genetic material must be limited in size, well-characterized, free of certain nucleotide sequences, and poorly mobilizable. Further explanation of the terms in (3) appears in Unit III.C.7. of this preamble.

In determining that the parent microorganism has a history of safe use, EPA would expect researchers to be able to classify taxonomically the microorganism and to evaluate its relationship with closely related microorganisms which may have a potential for adverse effects on human health or the environment. Information on the potential for the microorganism to cause adverse effects on human health and the environment should be evaluated.

EPA recognizes that a determination that a microorganism has a history of safe use involves a balancing of various factors. This determination should be premised on the researcher's prediction of the behavior of the microorganism based on experience with its use. The more information the researcher has on the behavior of the microorganism (for example, the ability to establish, compete, and survive in the environment), the better the researcher can estimate the safety of the field test. In conducting their risk assessment, researchers should consider the scale, since the tests must be conducted on 10 acres or less of land.

An additional requirement for this alternative exemption would be that an official having authority to represent the organization (e.g., the Chief Executive Officer, the General Counsel) certifies that the determination has been made by a TQI and is considered to be the official position of the organization. The official would also be required to state that the organization accepts full liability for all potentially harmful consequences of the field test. To show that relevant considerations had been evaluated, a TQI would be required to prepare a written analysis to be kept in the company's records. These records would be kept for 5 years from the date of the field test, with EPA retaining the right to review the records upon request. In lieu of a TQI, the analysis could be performed by a third party review group with relevant scientific expertise (i.e., ecological expertise) as exemplified by the Institutional Biosafety Committees (IBCs) described in the NIH Guidelines.

Following the TQI's determination, the researcher would be required to submit a short notice to EPA, providing the organization name and address, a summary of the new microorganism and the proposed field test, the name of the TQI, and the official certification, including the liability statement. EPA would have 45 days to determine whether to require submission of a TERA before the researcher could conduct the planned field test.

EPA requests comments on this alternative approach for low risk field tests. In particular, EPA would like to know whether there are other criteria which would be appropriate for defining a category of low risk small-scale field tests and what additional guidance would be needed

for researchers to utilize such an approach. The rationale for this alternative exemption is discussed in Unit III.C. of this preamble.

## III. Rationale for Proposed Reporting Mechanisms

### *A. Research for Commercial Purposes*

1. *Introduction*. TSCA section 5(i), while it limits all section 5 screening to activities for commercial purposes, has had little practical effect on research using traditional chemicals, because of the research exemption. However, because this proposed rule would place more requirements on research with microorganisms than on research with traditional chemicals, EPA believes it should provide its current view on the applicability of the commercial purposes limitation to this proposed rule.

As a preliminary matter, there is no difficulty in determining when any chemical substance, including a microorganism, is being manufactured or processed for a commercial purpose after the R&D stage. It is clear when a PMN is required or when a MCAN would be required at general commercial use.

Research on traditional chemicals is not generally affected by the commercial purposes limitation, because EPA's current regulatory definition of small quantities for R&D using traditional chemicals (any amounts reasonably necessary for research) at § 720.3 effectively exempts research with these chemicals from section 5 screening. However, as noted in Unit III.B. of this preamble, these rules propose a small quantities definition for microorganisms; and this definition, because it would recognize the ability of microorganisms to reproduce, would differ from the definition for traditional chemicals. A researcher utilizing microorganisms, therefore, may need to consider what constitutes a commercial purpose.

Research involving microorganisms used in contained structures would be considered ''small quantities solely for research and development'' as defined at § 725.3 of the regulatory text. Although EPA expects the requirements for this contained structures exemption simply to reflect common practices, a researcher may have to evaluate whether research conducted in contained structures is commercial. The contained structures exemption would not apply to field testing of microorganisms because of the ability of living microorganisms to reproduce and spread in the environment (see Unit III.B. of this preamble). As a result researchers will, in all cases, need to decide which environmental testing is commercial.

EPA wishes to emphasize that any coverage of research under this proposed rule should not duplicate appropriate oversight by other Federal authorities. As explained in Unit III.C.3. of this preamble, contained research appropriately overseen by other Federal agencies would be exempt from EPA oversight, because EPA believes such research does not present an unreasonable risk. As a practical matter, therefore, while testing conducted at institutions that do not normally consider themselves commercial (academic and non-profit institutions) could theoretically be commercial under interpretations discussed in this Unit, EPA anticipates that other parts of these rules will exempt much of the research from EPA oversight.

2. *Public comments*. During development of regulations on biotechnology, EPA has received numerous public comments that differ substantially on oversight of research. Of particular concern has been the appropriateness of EPA review based on the status of an activity as commercial rather than on its potential risk.

Comments argue that there is no reason to suspect any difference in risk between commercial or noncommercial research. Thus, if a university and a business release the same microorganism in similar settings, both should be subject to oversight.

On the other hand, comments suggest there may be risk differences. Some argue that a commercial enterprise is more likely to be careful than a noncommercial institution due to concern for liability. Others argue that academic researchers are more likely to be concerned with, and aware of, the need to consider health and environmental safety issues and that commercial entities may be willing to take shortcuts in the interest of reducing costs.

Other comments complain that increased government regulations may have a deleterious effect on academic research, because it may be more difficult for pure research institutions to comply. Burdens that are relatively minor for a business could be major for a university or an individual researcher.

Comments have also indicated that a number of practical difficulties increase the burden on research institutions. For example, increasingly complex and intermingled financial arrangements in the biotechnology field have emerged as universities seek funding from businesses. These arrangements may result in universities conducting product development for money or equipment donations from business. Undue burdens to academic researchers can result from requirements that research which is funded by a commercial entity be distinguished from that funded by a noncommercial entity, particularly when a university may pool its funds from various sources.

Finally, even though an academic research institution may engage in product development for a business, the institution may not be engaging in a commercial activity for its own benefit. For example, a university may use income from a commercial entity to improve its teaching and its ability to increase knowledge. Industry could be an important source of income for upgrading equipment used for teaching.

The remainder of this Unit discusses EPA's view of the law and

policy and responds to these public comments.

3. *EPA's view of the law as it applies to commercial activities at noncommercial institutions*. EPA wishes to make it clear that the interpretations discussed in this Unit are consistent with interpretations in current regulations. That is, a commercial activity is one undertaken with the purpose of obtaining an immediate or eventual commercial advantage. This is the common thread in § 720.3(r) which defines ''manufacture or import for commercial purposes'' and § 721.3 which defines ''process for commercial purposes.'' Similarly, § 720.30(i) provides that ''non-commercial research and development'' consists of activities conducted by academic, government, or independent not-for-profit organizations ''unless the activity is for eventual commercial purposes.''

All research conducted directly by a commercial entity is clearly for commercial purposes, as was decided in *The Dow Chemical Company v. EPA*, 605 F.2d 673 (3d Cir. 1979). Consequently, if a business directly funds a research activity for product development, the activity is for commercial purposes, regardless of the location. A business may not avoid review by simply funding research at an academic institution.

In section 5, Congress distinguished between commercial and noncommercial activities and, thus, expected them to be treated differently. Although the statute has no definitive explanation as to what this distinction means, it does not appear to have been risk-based. EPA believes that Congress did not provide a definitive explanation and therefore left to the Agency's discretion the balancing of competing interests. TSCA section 2(b) states that it is the policy of the United States that TSCA authority should be exercised so as not to ''impede unduly or create unnecessary economic barriers to technological innovation,'' while fulfilling the primary purpose of assuring that innovation does not present unreasonable risks.

If EPA considers that section 5 provides a screening mechanism, as opposed to a direct regulatory mechanism, EPA has an indication why the commercial purposes limitation applies. Under other TSCA provisions, EPA may regulate without regard to a commercial purposes limitation. For example, the commercial purposes limitation does not apply to EPA's authority under TSCA section 6 to prohibit or limit manufacture, processing, or distribution in commerce of chemical substances if the Agency finds that the particular activities present an unreasonable risk.

By providing a commercial purposes limitation for EPA to cover early phases of product development, Congress recognized the need for EPA to balance the competing interests of fostering innovation and protecting human health and the environment from unreasonable risk. In balancing these interests, EPA could construe the commercial purposes limitation to exclude relatively few activities during screening to cover a broad range of risk possibilities. Therefore, the broadest meaning of commercial purposes would miss hardly any research.

4. *Alternative interpretations affecting which activities at noncommercial institutions will be considered commercial*. Any of the three alternative interpretations of commercial purposes set forth below, as well as any other interpretation that is suggested by public comment and meets the intent of TSCA and adequately protects public health and the environment from unreasonable risks, may be adopted by the Agency in its final rule. Regardless of the alternative chosen, EPA would encourage researchers to voluntarily consult with EPA to find out if EPA considers their research to be commercial.

a. *Indicia of commercial purposes*. The usual way to interpret a statutory term of art like ''commercial purposes'' would be to look for indicia of commercial intent. This is what EPA does in its TSCA section 5 program for traditional chemicals. The Agency has not provided any detailed public discussion of what these indicia may be for traditional chemicals, but because the Agency will be reviewing R&D activities in its biotechnology program, a discussion of these indicia for the biotechnology program is appropriate.

While EPA may develop a general discussion, no exhaustive list of commercial indicia can be developed *a priori*. If EPA adopts this approach, the commercial indicia would apply to R&D in laboratories and other contained structures, as well as to intentional testing in the environment. Some environmental testing of new microorganisms would not be screened, because it would not be for commercial purposes.

EPA acknowledges that noncommercial institutions may find it difficult to trace funding for particular activities or to decide whether an activity is commercial or not. However, EPA supports this alternative, under the theory that the burdens of reporting to EPA are costs of doing business for any organization that wants the benefits of commercial financing. In addition, EPA believes that reporting at the research stage under this proposed rule does not impose an unnecessary burden on innovation and that the indicia described below would be consistent with the intent of TSCA. There are two general categories of commercial indicia for activities at nonprofit institutions; one involves industry involvement, either directly or indirectly; the other does not.

(i) *Direct industry involvement*. As noted above, any direct industry involvement in an activity at a noncommercial institution is for commercial purposes. Examples of direct commercial funding include situations in which a commercial entity contracts directly with a university, or gives a conditional grant where the commercial entity holds patent rights, or establishes a

joint venture where the commercial entity holds patent or licensing rights.

(ii) *Indirect industry involvement*. Indirect benefits to the commercial entity are not as clear. For example, a commercial entity may give a gift to a research institution with no limits on the use of the funds or research results. However, since the funds originated from a commercial source, a commercial purpose may nonetheless exist. Other indirect relationships between commercial and noncommercial entities need to be considered. For example, a commercial entity may guarantee a university bank loan for research, a faculty member associated with biotechnology research may have a financial interest in a biotechnology company, research may be conducted at a science park jointly owned by a university and commercial enterprises.

(iii) *No industry involvement*. If there is no industry involvement, EPA needs to look at the intent of the individual researcher or institution. Entrepreneurial faculty members may obtain financial rewards from their own inventions. Some may take out personal patents or derive personal income. The university may benefit from the patents or may sell products or services commercially, for example, to farmers. Because products may be sold to consumers, EPA is inclined to consider these activities commercial. However, if profits are used to support research or improve teaching facilities, EPA may recognize a case for considering the activity not to be commercial.

EPA could also consider activities supported by Federal or State government to be commercial. Many of these government activities are designed to foster economic benefits for particular groups, such as farmers. Also, the government may support university centers for technology transfer to industry. The issue may be philosophical, regarding whether government economic activities benefit individuals or the general welfare. EPA believes there are legitimate arguments for either view.

Finally, EPA may consider all activities at a nonprofit institution to be commercial if any activity is. Thus, if a company finances one activity at the university, all of the university's research may be considered commercial. If a university has an equity interest in a biotechnology company or a faculty member is associated with a firm, all the university's research activities may be considered commercial. This interpretation is supported by the fact that commercial activities free resources for noncommercial activities.

If EPA interprets all these situations strictly, for practical purposes, almost all research could be commercial. EPA notes for comment, however, not-for-profit institutions that obtain self-generated funds through charitable or religious donations and government grants for pure research to identify health or environmental hazards. These situations may not be commercial under any circumstances.

Regardless of the alternative chosen for environmental research, EPA would base its interpretation of commercial purposes for research qualifying for the contained structures exemption on the broad set of indicia discussed under this first alternative, in light of its belief that EPA requirements for contained commercial R&D are similar to requirements placed on academic researchers by the NIH Guidelines. See Unit III.B. of this preamble. Therefore, the second and third alternatives would apply only to research which does not qualify for the contained structures exemption.

b. *All environmental research is commercial*. Because of the ability of microorganisms to reproduce, disseminate and spread and the features of intentional testing in the environment, EPA believes it should propose another interpretation to address such testing. Under this interpretation, all intentional testing outside of contained structures would be commercial. This interpretation would avoid the most significant problem identified by comments, which is that there is no real difference in risk between research conducted by industry and by noncommercial entities.

As discussed more fully in Unit III.B. of this preamble, microorganisms function differently than other chemical substances. Because R&D involving the introduction of new microorganisms into the environment involves greater uncertainty than R&D involving use of microorganisms under contained conditions, EPA believes that a different position is warranted for intentional testing of microorganisms in the environment.

Because the TERA burden is structured to be minimal, EPA believes reporting will not seriously restrict academic R&D. In fact, this interpretation of commercial purposes in some respects could lessen the burden on universities, because they will not have to separate their industry funding from other funding that they may not consider commercial.

While considering all environmental releases to be commercial may seem contrary to the usual view, the actual status of funding for the biotechnology industry supports this interpretation. Research relationships in biotechnology are pervasive and take many forms. According to an Office of Technology Assessment (OTA) report,

> in recent years, the rapid proliferation of collaborations in biological research, involving partnerships between universities, industry and government, has greatly extended the frequency, scope and visibility of such activities. Attempts to commercialize biological techniques have occurred at an accelerated rate when compared to other fields, involving a greater range of commercial application than discoveries in most other disciplines. (Ref. 4, page 13).

Even the United States government is involved, under the Technology Transfer Act, in the commercialization of biotechnology,

having developed a technology transfer policy between universities and industry with the goal of developing commercially useful products. Nonprofit foundations also participate in activities for commercial purposes, often to finance other nonprofit activities.

c. *Rebuttable presumption of commercial activity*. The same arguments for the option that all environmental releases are commercial support the rebuttable presumption option. The rebuttable presumption is also supported by the need to distinguish commercial and noncommercial activities under TSCA. The above discussion of commercial indicia indicates the types of evidence that a researcher may present to rebut the presumption. However, EPA believes that this option would be burdensome to researchers, because it would require them to maintain evidence concerning sources of funding for each environmental experiment. EPA also believes that this approach would be less protective of public health and the environment, because it does not adequately address uncertainty about the behavior of new microorganisms in the environment.

d. *Voluntary consultation*. EPA recognizes that regardless of the interpretation of commercial purposes adopted for the final rule, it will be difficult to apply any one interpretation in all cases. For this reason, EPA would encourage persons who believe that they are engaging in non-commercial R&D to voluntarily consult the Agency before initiating testing of microorganisms that would be considered new if used for commercial purposes.

*B. Exemption for Research in Contained Structures*

This Unit explains EPA's reasons for exempting from section 5 screening R&D activities performed under conditions that would minimize the number of microorganisms emitted, or where appropriate prevent emission of microorganisms from structures such as pilot fermentation facilities, greenhouses, and laboratories. The R&D reporting process is discussed in Unit II.D. of this preamble.

1. *Background*. The statutory authority for this exemption is TSCA section 5(h)(3). Section 5(h)(3) exempts from section 5 screening chemical substances manufactured or processed in small quantities solely for R&D, and directs EPA to define small quantities by rule. Accordingly, proposed § 725.3 provides that R&D activities involving microorganisms would qualify for the section 5(h)(3) exemption when these activities are conducted under conditions designed to meet appropriate standards of containment and when employees are notified of risks. Some R&D activities which are eligible for the contained structures exemption may also be subject to the jurisdiction of another Federal agency. In these cases, EPA proposes to defer to the authority of the other Agency. The rationale for this proposed deferral is discussed in Unit III.C.3. of this preamble.

2. *Difficulties in ensuring that microorganisms used for R&D will not increase beyond small quantities*. EPA's current regulations for traditional chemicals at § 720.3(cc) define ''small quantities solely for R&D'' as those quantities that are ''not greater than reasonably necessary for ... [R&D] purposes.'' This definition of small quantities for R&D has been appropriate for traditional chemical substances, because these chemicals do not have the ability to increase their own volume or amount. To the extent a finite amount of a traditional chemical released during an experiment may leave a test site, it will only be diluted in the environment.

Living microorganisms are not, however, subject to these same limitations. Microorganisms may reproduce and increase beyond the number initially introduced, may establish in the environment (i.e., develop a self-sustaining population), and may spread beyond the test site. Thus, what begins as a small, localized population of microorganisms may become a large, widespread population. Even if certain microorganisms do not exhibit the ability to reproduce, increase in number, establish, and spread beyond the test site, they may be capable of passing some of their traits to other microorganisms in the environment. These other microorganisms may, in turn, multiply, establish, spread and subsequently pass the acquired trait to other microorganisms. This could result in widespread propagation of the trait, and exposure of a number of different environments to novel traits.

These abilities of living microorganisms render the general definition of small quantities that applies well to traditional chemicals invalid for microorganisms. If the definition developed for traditional chemicals was applied to living microorganisms, EPA would not review microorganisms until they were produced for general commercial use. New microorganisms could be released, with no EPA review, during R&D testing in the environment, perhaps numerous times, and could become established and spread. This would defeat the purpose of TSCA, which is designed to permit EPA to review chemical substances before they become widely disseminated.

Consequently, a determination of what constitutes small quantities for microorganisms requires that more factors be taken into consideration than are considered for traditional chemicals. These factors revolve around the probability that a microorganism will establish itself in the environment. Establishment is a key consideration, because unless a microorganism establishes, any effects it might have would probably be spatially and temporally limited. Several factors influence whether a microorganism will be able to establish itself. These include the numbers of microorganisms involved, the frequency with which

they are applied to the area, the method of application, the characteristics of the microorganism, the physiological condition of the microorganism at the time of application, and the characteristics and condition of the receiving environment.

Case histories of both disease epidemics and invasions of higher organisms suggest that the number of organisms present in the inoculum directly influences whether the introduction yields a self-sustaining population (Ref. 5). Experience with microorganisms used in biocontrol (i.e., purposeful use of microorganisms as antagonists to reduce the disease-producing ability of plant pathogens) has shown that success in some instances can be enhanced if a large number of the biocontrol microorganism is introduced (Ref. 6).

It can be inferred from this information that the number of organisms, both with regard to the density of the inoculum and the geographic range over which it is introduced (Refs. 7 and 8), is related to probability of establishment. Several hypotheses on why this may be so can be offered. In some cases, mortality in the introduced population can be overcome if the inoculum contains a large number of individuals. In other situations, a large inoculum population may provide sufficient genetic variation that individuals that can tolerate or prosper in the environment of introduction will be within the inoculum (Refs. 9 and 10). A biocontrol strategy that relies on the inoculum containing large numbers of microorganisms is thought to be successful because the introduced microorganisms may by sheer numbers have an advantage in reaching and filling available suitable microhabitats, availability of suitable habitat being a limiting factor for any population of organisms.

The frequency with which organisms are released to an environment also affects whether an organism can establish. Frequent releases increase the likelihood that the microorganism will find sites favorable for establishment by increasing the total number of microorganisms placed in the environment and by increasing the probability that a microorganism will be introduced during a time favorable for establishment. This latter probability is related to factors such as the variations in temperature, moisture, light, and biota observed with seasonality. In other words, conditions favorable for establishment may exist at some period of time and not at others, and frequent application increases the probability that some individuals will be at the right place at the right time.

3. *Regulatory conditions to prevent microorganisms used for R&D from increasing beyond small quantities*. EPA's proposed standards at §§ 725.234 (containment and recordkeeping) and 725.235 (employee notification) are designed to reduce the probability of establishment by reducing the number and frequency of viable microorganisms emitted from a facility. The reduced probability of establishment increases the probability that a microorganism will remain a small quantity.

EPA is proposing performance-based standards for this exemption. EPA's approach relies on the experience and judgement of the TQI, and EPA will not generally substitute its own judgement for that of the TQI. The approach recognizes that many different kinds of microorganisms displaying a wide range of characteristics could potentially be used in research, and that for certain microorganisms, emission of only a few viable individuals could cause an effect, while emission of large quantities of viable microorganisms of another type would not. It also recognizes that the type of controls (e.g., procedural, mechanical, and/or engineering) appropriate for one microorganism might have limited relevance to other microorganisms. EPA expects that the TQI will be cognizant of these factors when selecting containment and inactivation controls appropriate to the microorganism(s) being utilized.

EPA does not believe the documentation requirements proposed for this exemption will be overly burdensome. EPA believes that for most cases, laboratory notebooks normally kept in the course of research will contain most of the information required by this proposal. Control measures selected could be indicated by reference to existing standards (e.g., one of the containment levels described in the NIH Guidelines). The TQI would simply record the reasons for choosing particular measures. With regard to the requirement that records document use of the selected controls, EPA is relying on the TQI to prepare and retain the appropriate degree of documentation. The amount of documentation would be correlated with the characteristics of the research microorganism and standard practices employed to address risk. Thus, documentation could range from general documentation of routine standard operating procedures, to specific notations in laboratory notebooks, to daily log entries for microorganisms that present the greatest risk concerns. If the NIH Guidelines are used as guidance, the TQI's notebook should indicate the level of containment recommended by the Guidelines and that this guidance was selected and used. EPA believes that persons following the NIH Guidelines would keep adequate records as part of normal procedures for informing their Institutional Biosafety Committee of the contained research.

With respect to the certification requirement, many if not most research institutions have Institutional Biosafety Committees (IBCs) as required by the NIH Guidelines, or committees fulfilling a similar role. These committees are charged with assessing the containment selected by the investigator. EPA recognizes the

value of this NIH system and would like to make its requirements consistent to the extent possible with such existing systems. The Agency also encourages the active use of such committees.

The provision which indicates that EPA may request these records be sent to EPA for review (see § 725.234(d)(3) of the regulatory text) is a restatement of the authority EPA has under TSCA section 11 to request and review information. It is also similar to provisions used by EPA in other exemptions. In the three exemptions from PMN reporting under part 723 that currently exist for traditional chemicals, one of the conditions for eligibility for the exemptions gives EPA access to the records demonstrating eligibility for the exemptions. EPA can require a company to produce the records upon EPA's written request.

EPA does not plan to routinely review such records, although it may choose periodically to select some records for review. Should the institution or researcher receive a request for records review, the status of the research as exempt would not *a priori* be affected. Technical staff with experience reviewing TERA and MCAN submissions would examine the records. This provision allows EPA and the researcher to discuss what constitutes appropriate control measures and appropriate implementation and use. Under this provision, EPA may, upon review of the records, offer recommendations concerning what it considers appropriate control measures for the specific microorganisms used in the research. These recommendations would be non-binding. If EPA determines, however, that the control measures selected and used are so inadequate as to present an unreasonable risk, EPA can issue an order directed at modifying the control measures it finds problematic. Refusal to comply with an order would result in loss of eligibility for the exemption for the research in question. The researcher would then be subject to the notification requirements of TSCA section 5.

EPA's criteria at proposed §§ 725.234 and 725.235 are designed to reduce the probability of establishment by reducing the number of viable microorganisms emitted from a facility. However, EPA's proposed approach also takes into consideration factors such as the physiological condition of the microorganisms and how this might affect the ability of microorganisms to establish in the environment. Microorganisms used in laboratory research are more likely to be debilitated with regard to their ability to compete in the environment against wild type relatives. Thus, they may be less likely to prevail in the struggle in nature for limited resources. In general, incidental releases of microorganisms from research facilities are less likely to occur under conditions which favor the establishment of the microorganism. Incidentally released microorganisms may be physiologically debilitated by aerosolization or other process procedures, and may be less likely to find an environment that favors their survival and persistence than those microorganisms that are specifically tested in an environment where they are intended to survive, at least long enough to perform a specific function.

EPA recognizes that parts of the rationale offered for exempting research conducted under the conditions set forth in proposed § 725.234 can be applied to some small-scale field tests involving microorganisms. The rationale cannot, however, be applied to small scale field tests as a class. Microorganisms intentionally tested in the environment are more likely to be acclimated to the environment into which they are introduced, be physiologically fit enough to be competitive in that environment for a significant period of time, and be placed in an area suitable for growth and persistence. Because of the lessons learned with biocontrol microorganisms, researchers will purposefully apply large enough numbers to ensure that the microorganism persists long enough and competes well enough to perform the function the researcher intends to study. In general, the probability that these types of microorganisms, used under these conditions, will establish is thus higher than the probability associated with incidental emissions from facilities employing EPA's proposed criteria.

4. *Alternative reasons for the research exemption.* An alternative rationale would hold that the small quantities exemption in section 5(h)(3) does not apply to microorganisms as a class, because some microorganisms, whether they are released through intentional testing or incidental emission, can establish even though the initial inoculum is very small. For some microorganisms, a single microorganism may be a sufficient inoculum for establishment to occur. Thus, for microorganisms as a class, there can be no concept of ''small quantities'' similar to that envisioned for other chemicals.

EPA would find, however, that research conducted under the criteria specified in §§ 725.234 and 725.235 could be exempted under TSCA section 5(h)(4). EPA's authority under TSCA § 5(h)(4) is discussed in Unit III.C. of this preamble. In situations where the EPA criteria at §§ 725.234 and 725.235 are followed, EPA believes that the resulting reduction in the number of microorganisms emitted from R&D facilities will reduce the probability that a microorganism will establish in the environment. This reduced probability of establishment leads directly to a reduction in risk. If a microorganism does not establish, its ability to present risk is far less likely to be expressed. If the microorganism is not able to establish, any adverse effects that might be associated with that microorganism will probably be spatially and temporally limited.

EPA recognizes that some research activities may present special

considerations; e.g., when the research utilizes microorganisms that can successfully establish from a very small inoculum. In such cases, incidental emission from the facility may have to be much more stringently controlled to reduce risk. EPA believes that its requirement that a technically qualified individual (TQI) select and validate procedures appropriate to the microorganism addresses this concern. That person should select, validate, and follow procedures that would ensure that insufficient numbers of viable microorganisms are emitted from the facility for establishment to occur.

EPA believes that any potential risk presented by incidental releases from research facilities that might occur, even when its criteria for reducing the number of microorganisms emitted from the facility are followed, is outweighed by the benefits to society of biotechnology research. EPA can use its limited resources, which otherwise would be used to review these low risk research activities for microorganisms, for reviewing higher risk activities and microorganisms. Industry, by having this exemption, can develop and test microorganisms in the early stages of the product development process (e.g., laboratory) without having to be reviewed by EPA. This would reduce the time and cost for industry in developing new products. More time and resources could be allotted for actual R&D and less time and resources allotted to EPA notifications. This should assist the development of this industry and the emergence of new, useful products, and thus not present an unreasonable risk of injury to human health and the environment.

5. *Alternative methods of reducing the number of microorganisms emitted*. EPA believes its proposed approach to reducing the number of microorganisms emitted from research facilities is preferable to more prescriptive approaches which have been suggested. The suggested approaches include setting a specific numerical standard for the number of microorganisms that might be incidentally released to the environment from a research facility, prescribing a single standard based on one of the containment levels described in the NIH Guidelines, or an approach wherein several increasingly stringent levels of containment are described and specific microorganisms are matched to specific levels. These three approaches would be complex and unwieldy to implement. Because of their prescriptive nature, such approaches would result in EPA regulating the containment standards rather than exempting the research. This would unnecessarily restrict research contrary to the intent of TSCA. Each change to a prescriptive standard would have to be incorporated into the standards through rule amendments or variance procedures. Establishing prescriptive standards could restrict advances in technology for controlling microorganisms and stifle individual initiative at the research level.

*C. Section 5(h)(4) Exemptions*

1. *Introduction*—a. *Statutory background*. Section 5(h)(4) of TSCA provides that EPA may exempt by rule the manufacture of any new chemical substance from all or part of the requirements of section 5, if it is determined that activities involving the substance will not present an unreasonable risk of injury to health or the environment. A section 5(h)(4) rule must be promulgated under the procedures set forth in TSCA sections 6(c)(2) and (3), which generally require preparation of a rulemaking record and an administrative hearing. EPA is proposing to use section 5(h)(4) to support various exemptions from the notification requirements of the rule.

The term ‘‘unreasonable risk’’ is not defined in TSCA. Section 6(c) of TSCA lists considerations for determining whether a chemical substance presents an unreasonable risk for purposes of promulgating regulations under TSCA section 6. These considerations include the effects of the substance on human health and on the environment and the magnitude of exposure to the substance, the benefits of the substance for various uses, the availability of substitutes for such uses, and the reasonably ascertainable economic consequences of the potential regulatory action, considering effects on the national economy, small business, technological innovation, the environment, and public health. EPA believes it is reasonable to consider these factors in determining whether a risk is unreasonable under section 5(h)(4).

TSCA offers no further direct guidance on what constitutes unreasonable risk. In particular, TSCA does not discuss how each of the section 6(c) considerations are to be weighed in relation to each other. The legislative history, therefore, needs to be considered. The House Report (H.R. Rep. 94-1341, 94th Cong., 2d Sess. at 13-15, 32) provides the most useful pertinent explanation. First, the standard under TSCA is ‘‘unreasonable’’ risk, not a decision to eliminate all risk (House Report at 15). For an activity that is of some value to society, some level of risk may be acceptable. With respect to section 5(h)(4), granting an exemption does not require a showing that there will be no risk, only that there will be no unreasonable risk.

The House Report states that the unreasonable risk standard cannot be defined in precise terms but, instead, requires exercise of judgment by the decisionmaker. The House Report describes the finding of unreasonable risk as involving a balancing of the probability that harm will occur, and the magnitude and severity (potential consequences) of that harm, against the effects (social and economic) of proposed action on society.

According to the House Report, these evaluations of harm often must be based on considerations of ‘‘scientific theories, projections of trends from currently available data,

modeling using reasonable assumptions, and extrapolations from limited data'' (House Report at 32). The unreasonable risk standard recognizes that, as a practical matter, all the scientific evidence is uncertain to some degree and that EPA can consider such factors as the strength of the evidence on toxicity, the nature of the effects that may occur (e.g., death vs. reversible effects), and the likely numbers of individuals exposed and the levels of exposure.

The House Report points out that the unreasonable risk standard is flexible enough to allow EPA to calibrate the stringency of a regulatory measure to the levels of risks and benefits. Thus, a testing rule, because it does not deprive the public of the benefits of a chemical, requires a lesser showing of harm compared to a rule which may remove a substance from the market or impose other restrictions on its availability. Similarly, a stronger showing would be required to ban an activity than to impose lesser restrictions on use or a requirement, such as labelling, that does not restrict directly.

The greater the probability and the more severe the potential harm presented by an activity EPA may allow, the less likely a no unreasonable risk finding can be made. Similarly, the greater the benefit of the activity, the greater the risk to be tolerated. Determinations of whether an exemption should be partial or full will depend on the probability and severity of the harm and the benefits to be derived from the activity. Less restrictions should apply if there are substantial benefits from the activity and the probability of harm appears to be lower or the consequences are of low concern.

b. *Summary of section 5(h)(4) exemptions*. EPA is proposing to use its authority under TSCA section 5(h)(4) to establish six separate types of exemptions. These are partial exemptions that involve limited reporting and/or recordkeeping for new microorganisms that meet the eligibility requirements of the specific exemptions. Five of these exemptions specifically relate to R&D activities. The sixth case is a tiered exemption for general commercial use.

Because each exemption involves a different set of issues, each exemption requires a different weighing of risks and product benefits. The remainder of this unit sets out the no unreasonable risk findings for each of the exemptions. For each exemption, a review of the relevant scientific risk considerations is followed by a discussion of the social and economic benefits resulting from microbiological products. The extent to which both risks and benefits are considered is dependent on the breadth of the exemption.

2. *Alternative finding of no unreasonable risk for microorganisms used for R&D in contained structures*. The reasoning for this alternative finding relies on the factors discussed in Unit III.B. of this preamble for research that meets the criteria at proposed §§ 725.234 and 725.235 for R&D conducted in contained structures. See Unit III.B. of this preamble for a full discussion of the rationale for exempting research in contained structures.

3. *Deferral to other Federal authorities for oversight of R&D*. Unit II.D. of this preamble describes a proposed exemption from this regulation for research controlled by other federal authorities. This section provides EPA's reasons for establishing this exemption. The exemption is based on the general policy that TSCA should not apply to research adequately overseen by other federal authorities.

TSCA jurisdiction is discussed in Unit I.C. of this preamble. Generally microorganisms controlled by other Federal agency authorities, other than those microorganisms regulated under FIFRA or FDA authorities, are also subject to TSCA. Agencies, such as the Animal and Plant Health Inspection Service (APHIS) of the U.S. Department of Agriculture (USDA), have regulatory authority that overlaps TSCA authority for microorganisms. Research subject to TSCA may also be funded by Federal agencies, such as the Department of Defense (DOD), the Department of Energy (DOE), the National Institutes of Health (NIH), the National Science Foundation (NSF), USDA's APHIS or its Office of Science and Education (S&E), or EPA's own Office of Research and Development (EPA/ORD).

On November 23, 1976, all Federal agencies represented on the Federal Interagency Committee endorsed the NIH Guidelines. Departments which support or conduct laboratory rDNA research agreed to abide by the Guidelines in June 1983 (48 FR 24577). Because of the 1983 agreement, as a condition for Federal funding of rDNA laboratory research, institutions must ensure that all rDNA research conducted at or sponsored by the institution, regardless of the source of the funding, complies with the Guidelines.

a. *Finding of no unreasonable risk for R&D in contained structures subject to the authority of other Federal agencies*. This proposed rule would provide an exemption for research in contained structures (principally laboratories) covered by the NIH Guidelines. EPA considers the NIH Guidelines to provide the primary standard for laboratory research. EPA's rules are designed to provide complementary oversight of those activities not covered by NIH. As a result, EPA is proposing a complete exemption under TSCA section 5(h)(4) for research on new microorganisms in contained structures, if the researcher is required to comply with the NIH Guidelines. This may be achieved through direct regulatory authority or through requiring recipients of Federal funds to comply with the NIH Guidelines. Without this exemption, the recordkeeping and employee notification requirements of proposed §§ 725.234 and 725.235 would apply to this research. EPA's summary analysis of the NIH Guidelines may be found in the

docket which supports this rulemaking.

EPA proposes under TSCA section 5(h)(4) to exempt from the requirements described in proposed §§ 725.234 and 725.235 the manufacturers, producers and importers of new microorganisms for R&D in contained structures, if the research is regulated or funded by a Federal agency which has agreed to abide by the NIH Guidelines.

The pertinent parts of EPA's regulations applying to R&D in contained structures are § 725.234(b) and (d). They require a technically qualified individual (TQI) to maintain documentation that describes the selection of containment and inactivation procedures and ensures the procedures are followed. The TQI's selections must be approved and certified by an authorized official of the institution conducting the experiment (§ 725.234(d)(2)). EPA may request the records, review containment/inactivation controls and may order changes in containment/inactivation procedures (§ 725.234(d)(3) and (d)(4)).

These provisions are designed to complement the NIH Guidelines and extend their benefits, without imposing an overly rigid regulatory regime. EPA's regulation is in the same spirit as the NIH Guidelines in that it is also based on the fact that all conceivable experiments cannot be foreseen and that it is the responsibility of the experimenting institution to devise appropriate containment. Like NIH, EPA emphasizes the importance of the motivation and good judgment of the investigators.

Because the NIH Guidelines are very well entrenched in the research community, EPA expects that the procedures chosen by the TQI will very closely follow the Guidelines. In addition, any EPA review of records will rely heavily on the Guidelines. Thus, by establishing the provisions of proposed § 725.234(d), EPA would effectively apply Guideline principles to those institutions, primarily commercial facilities, that are not required to abide by them. This would complement the NIH request for voluntary compliance.

Further, the NIH Guidelines apply directly only to those microorganisms, and categories of microorganisms, that have been listed in the Guidelines and, in particular, Guideline Appendices A through F. Other microorganisms would require specific review by NIH. EPA regulations extend the benefits of the NIH Guidelines by effectively applying their principles to microorganisms other than those specifically mentioned in the Guidelines.

At the same time, by not incorporating the Guidelines directly into regulations, EPA would avoid overly rigid adherence to Guidelines that are, themselves, meant to be flexible. EPA, however, retains sufficient control to protect against risk by the review procedures in proposed § 725.234(d)(3) and (d)(4).

Requiring researchers to adhere to the proposed requirements of §§ 725.234 and 725.235 as well as to the requirements of these other federal authorities would be a duplication of oversight and enforcement that would unnecessarily restrict potentially beneficial research without any incremental reduction in potential risk. Thus, there would be no increase in risk from removing the TSCA section 5 restrictions placed on contained structure R&D. Further, costs will be reduced, because there would be no costs incurred in complying with TSCA. R&D would be encouraged without an attendant increase in risk. Therefore, the risks of exempting this research from the TSCA section 5 contained structure R&D restrictions are far outweighed by the costs saved. Accordingly, EPA finds there will be no unreasonable risk from this exemption.

b. *Federal agency R&D subject to TERA reporting*. EPA has also considered how it might use its TSCA section 5(h)(4) exemption authority to minimize duplicative reviews of environmental release tests that are also subject to other Federal agencies. EPA has determined that a different exemption process should apply to experiments in the environment than to contained experiments. While the NIH Guidelines are recognized as a standard for contained R&D, the same situation does not pertain to R&D activities involving releases to the environment. Accordingly, EPA is planning to propose the procedures outlined below for exemptions from the TERA process for deliberate release experiments reviewed by other Federal agencies.

With agencies that have clear regulatory authority, EPA would propose to exempt from TSCA section 5 requirements intentional environmental testing of new microorganisms and to defer to the other Federal agency's review, when EPA determines that the other Federal agency's review addresses criteria equivalent to those which would be evaluated under TSCA section 5. When EPA develops such an exemption involving deferral to another Federal agency, it will propose the exemption using notice and comment rulemaking. EPA is currently working with USDA-APHIS to develop an exemption for R&D field tests reviewed by APHIS under the Federal Plant Pest Act and the Plant Quarantine Act and implementing regulations at 7 CFR part 340 and hopes to include such an exemption when the rule is promulgated.

4. *Finding of no unreasonable risk for TERA approval of new microorganisms*—a. *Background*. EPA recognizes that many small-scale tests will not present unreasonable risks and that requirements restricting R&D could stifle innovation contrary to the intent of TSCA. Therefore, under section 5(h)(4) EPA is proposing to conditionally exempt from MCAN notification R&D involving certain new microorganisms. The exemption is conditional, since researchers must submit a TERA.

EPA's current experience with reviewing PMNs for microorganisms used for R&D in the environment

under the 1986 Policy Statement has indicated that EPA could more efficiently review these activities. While the current process provides an adequate mechanism, R&D activities present a very different risk assessment situation than general commercial use. Differences in exposure, the ability to apply procedures for controlling routes of exposure or dissemination and the procedures for controlling potential risks, and the need for flexibility in R&D comprise different risk assessment scenarios than found in general commercial use. As a result, in light of these different scenarios, a more straightforward and flexible approach to reviewing experiments for new microorganisms is indicated. The TERA provisions of this proposed rule will provide such an approach.

A TERA provides for submission of information commensurate with the nature of the R&D process, because the review is focused on a specific R&D activity. Therefore, not as much information is required compared to a MCAN. For example, persons who submit a TERA would not have to include information on all commercial manufacture, processing, transport, use, and disposal activities that may involve the new microorganism as is the case for a MCAN.

The more flexible deadlines and procedures for the TERA would avoid unnecessary delays or restrictions on experiments. TSCA imposes a 90–day waiting period for section 5(a)(1) screening; and persons who submit MCANs must wait at least 90 days before an activity can begin, even if EPA should determine no unreasonable risk is posed by the activity before the 90–day review period expires. A similar waiting period may not be appropriate for experiments when more rapid decisions can be made. If TERA review shows that an experiment poses little or no risk, EPA could notify the submitter to proceed at any time during the review period prior to expiration of the review clock.

b. *No unreasonable risk determination.* EPA has decided that case-by-case review is required to determine the potential risk presented by a microorganism which may establish in the environment during the course of a field trial. The review would allow EPA to determine if it would be necessary to set limitations to minimize the probability of establishment and dissemination in the environment. Microorganisms intentionally tested in the environment are more likely to be acclimated to the environment into which they are introduced, be physiologically fit enough to be competitive in that environment for a significant period of time, and be placed in an area suitable for growth and persistence. Researchers generally apply large numbers of microorganisms to ensure that they persist long enough and compete well enough to perform the function the researcher intends to study. This fact increases the probability that microorganisms used under these conditions could establish and possibly pose a risk or result in significant exposure. Therefore EPA has concluded that R&D which involves intentional testing of microorganisms in the environment should be subject to some review.

EPA has balanced a number of considerations to determine that experiments reviewed under a TERA will not present an unreasonable risk to health or the environment and should be exempt from MCAN requirements. First, TERA review should result in no greater risks than those that might occur as a result of the MCAN process, because the no unreasonable risk criteria for approval are the same for either process. Second, TERA review may even reduce risks in some instances by allowing EPA to focus resources on activities that may pose the greatest potential for risk. Third, TERA review will reduce reporting costs by eliminating Agency need for information and procedures that are unnecessary for R&D. Fourth, when compared to the MCAN process, TERAs should encourage technological innovation and have a beneficial effect on small businesses engaged in R&D utilizing new microorganisms.

5. *Finding of no unreasonable risk for microorganisms proposed for exemption from TERA reporting*. EPA recognizes that some field experiments with new microorganisms do not need to be reviewed at all. EPA therefore intends to exempt from review some R&D experiments with certain new microorganisms. EPA will, however, still review any general commercial uses of these new microorganisms through the MCAN process. The no unreasonable risk finding for exemption from TERA reporting is based on the interaction of three principal criteria addressing the recipient species, the introduced genetic material, and procedures for limiting exposure during experimental use. The three criteria must be considered in concert, because any potential concerns raised in one set of criteria may be balanced or compensated by other criteria. These criteria are discussed in more detail in Unit III.C.7. of this preamble.

EPA requests comment on whether this approach should be used to exempt from TERA screening certain new microorganisms. EPA is proposing certain intergeneric strains of *Bradyrhizobium japonicum* and *Rhizobium meliloti* as candidates for exemption from TERA review, based on reviews of voluntary PMNs submitted under the 1986 Policy Statement and field test data generated in these field trials. Persons possessing information which they believe would support an exemption from TERA reporting for other new microorganisms may use the procedures in proposed § 725.67 to apply for such an exemption.

EPA proposes to list *Bradyrhizobium japonicum* and *Rhizobium meliloti* as acceptable recipient species. Both are well-

characterized taxonomically and have been used in the environment for over 80 years to improve nitrogen fixation in specific agricultural crops. There is extensive information on these two species documenting the lack of adverse effects in the environment, and no reports exist that they are pathogenic to humans or animals. In addition, EPA has reviewed field test data from several experiments which have demonstrated that the intergeneric strains are similar to the unmodified parental strains in colonization, survival, nodulation and effects on plant growth. The public dockets pertaining to the reviews of *B. japonicum* (six strains: P88–1275 through 1278, and P89–340 and 341) and *R. meliloti* (18 strains: P87–568 through 570, P88–1115 through 1122, P89–280, P90–339, and P92–399 through 403), along with the field test data, are incorporated into the docket for this rulemaking. These strains were modified in antibiotic resistance traits, and some were modified for nitrogen fixation traits as well. In the course of these reviews, EPA evaluated general and specific information in the open scientific literature concerning these species, and BSAC subcommittees were convened to discuss general issues associated with the proposed R&D experiments with these strains.

Modification of traits, the second criterion, limits the source of the introduced genetic material to the genera of *Rhizobium* and *Bradyrhizobium* but allows the introduction of antibiotic resistance traits from any source organism. In addition, the introduced genetic material must be poorly mobilizable. The introduction of genetic material for traits other than antibiotic resistance is limited to *Bradyrhizobium* and *Rhizobium* species, because EPA is most familiar with these two genera.

Based on the results of the field tests with these strains, EPA proposes to exempt the use of well-characterized, limited in size, and poorly mobilizable antibiotic resistance markers in *Bradyrhizobium japonicum* and *Rhizobium meliloti*. EPA believes that there would be no significant risk resulting from small-scale field tests with the resulting microorganisms containing antibiotic resistance, because broad antibiotic resistance already exists in naturally occurring microorganisms of these two species (as demonstrated in the data submitted for PMNs P88–1115 (rhizobia) and P88–1275 (bradyrhizobia). In addition, higher levels of antibiotic resistance can be easily induced in these microorganisms by mutation or selection. EPA requests comment on the appropriateness of exempting antibiotic resistance traits.

EPA is proposing that these exemptions would only apply to test sites of 10 acres or less. This test area limit for *Bradyrhizobium japonicum* and *Rhizobium meliloti* is based on the field data reviewed by EPA which show that such releases have remained small-scale, with the modified strains exhibiting survival and persistence similar to their unmodified parental strains. The TQI must select appropriate methods to limit dissemination of these modified rhizobial species in order to maintain the small-scale nature of the field tests. Also, this proposal is based on the lack of adverse effects observed in humans and animals resulting from use of these naturally occurring rhizobial species.

EPA is proposing to exempt intergeneric strains of these two rhizobia species, in order to facilitate research using these microorganisms and to encourage development of products that could increase crop productivity while decreasing dependance on chemical fertilizers. These experiments could generate important information that will increase understanding of the environmental fate of intergeneric microorganisms. Information from these field tests would advance the understanding of microbial ecology, which could facilitate review of commercial products. The possible risks due to exempting these two rhizobia species from review at small-scale will be balanced by the innovation and development of safer, environmentally sound products to promote crop production.

6. *Finding of no unreasonable risk for specific alternative exemption for low risk field tests*. Unit II.D. of this preamble describes an alternative exemption from TERA reporting for certain R&D field tests. While EPA acknowledges that parts of the rationale offered in Unit III.B. of this preamble for exempting research conducted under the proposed contained structures exemption could be applied to some small-scale field tests involving microorganisms, EPA does not believe that the rationale can be applied to small-scale field tests as a class. Therefore, it was suggested that EPA define a class of small-scale field tests which would be expected to pose low risks and be exempt from TERA reporting. The no unreasonable risk finding for this alternative exemption from TERA reporting is based on the interaction of three primary criteria which consider the safety of the parent microorganism, the role of the traits that have been modified, and the scale of the field tests. If the parent microorganism is shown to have a history of safe use, introduced genetic material meeting the specified criteria would be unlikely to significantly increase the potential for adverse effects. EPA would expect that TQIs would use the criteria discussed in III.C.7. of this preamble for the recipient microorganism and the introduced genetic material as guidance in determining that their new microorganisms would be eligible for this exemption. As in the contained structures exemption for R&D, EPA is relying on the experience and judgement of the TQI to select appropriate methods to limit dissemination of the new microorganisms in order to maintain the small-scale nature of the field tests. Reliance on the judgement of the TQI is discussed further in Unit III.B. of this preamble. EPA believes

that the criteria it has specified circumscribe a category of field tests which can be considered low risk. In addition, should EPA receive a notice for a planned field test which did not appear to be low risk, EPA could require the submission of a TERA in order to review more completely the proposal.

EPA believes that the field tests potentially eligible for this alternative exemption could generate important information which will generally advance the understanding of microbial ecology and specifically facilitate EPA's review of intergeneric microorganisms. The low risks posed by the field tests will be balanced by benefits in the form of reduction in reporting burden for researchers and the encouragement of innovation in the development of environmentally sound products. EPA would like to receive public comment on whether the benefits of this exemption outweigh the potential risks posed by small-scale field tests eligible for the exemption.

Although field tests which meet the proposed criteria would be considered to pose low risks, additional concerns could be raised for unlimited uses of the same microorganisms at the general commercial use stage. Once development of these microorganisms moves beyond R&D to general commercial use, they would be subject to the MCAN reporting requirements discussed in Unit II.C. of this preamble.

7. *Finding of no unreasonable risk for new microorganisms eligible for tiered commercial use exemption.* EPA recognizes that some microorganisms present a low risk when used under specific conditions at general commercial use. Therefore, EPA is proposing expedited processes for certain microorganisms at the general commercial use stage. The requirements and processes for the Tier I and Tier II exemptions are discussed in Unit II.C. of this preamble. The criteria for Tier I and Tier II exemptions address: (1) The recipient microorganism; (2) the introduced genetic material; and (3) performance based standards for minimizing the numbers of microorganisms emitted from the manufacturing facility.

To evaluate the potential for unreasonable risk to human health or the environment in developing these exemptions, EPA focused primarily on the characteristics of the recipient microorganisms. If the recipient is shown to have little or no potential for adverse effects, introduced genetic material meeting the specified criteria would not likely significantly increase potential for adverse effects. As further assurance that risks would be low, EPA is also specifying procedures for minimizing numbers of organisms emitted from the facility. When balanced against resource savings for society and expected product benefits, these exemptions will not present unreasonable risks.

a. *The recipient microorganism.* Six criteria were used to determine eligibility of recipient microorganisms for the tiered exemption. First, it should be possible to clearly identify and classify the microorganism. Available genotypic and phenotypic information should allow the microorganism to be assigned without confusion to an existing taxon which is easily recognized. Second, information should be available to evaluate the relationship of the microorganism to any other closely related microorganisms which have a potential for adverse effects on human health or the environment. Third, there should be a history of safe commercial use for the microorganism. Fourth, the commercial uses should indicate that the microorganism products might be subject to TSCA jurisdiction. Fifth, studies are available which indicate the potential for the microorganism to cause adverse effects on human health and the environment. Sixth, studies are available which indicate the survival characteristics of the microorganism in the environment. EPA requests comment on whether these are the appropriate criteria to consider to determine the eligibility of recipient microorganisms for the tiered exemption. After each microorganism was reviewed using the six evaluation criteria, a decision was made to place the microorganism on the list in proposed § 725.420. Summaries of the individual risk assessments, are discussed below. The full risk assessments for the recipient microorganisms are in the docket for this proposed rulemaking.

(i) *Acetobacter aceti* is an obligate aerobic bacterium naturally found in the restrictive niche of fermenting fruit, where it can tolerate and utilize ethanol as a nutrient. This species has no recorded pathogenicity on plants, humans, or animals and has a history of safe industrial use. *A. aceti* is well-defined taxonomically and clearly distinguished from other *Acetobacter* species known to cause the browning of processed fruit. While it can be expected to survive in the environment, *A. aceti* is unlikely to cause any significant environmental effects.

(ii) *Aspergillus niger* is an asexual fungus commonly found degrading organic matter in nature. This organism has a history of safe use for the production of citric acid and several enzymes. It has been shown to be an opportunistic human pathogen and to damage several species of plants. While production of certain mycotoxins has been associated with strains of *A. niger*, companies have been using naturally occurring strains of *A. niger* to produce a variety of products for many years without reports of toxic effects of workers. The limited in size constraints as well as the restriction on vertebrate toxins imposed on introduced genetic material by the criteria for the tiered exemption should reduce the likelihood of increased production or exposure to malformins A and C, the two most potent mycotoxins potentially produced by *A. niger* strains. In general, the restrictions placed on the introduced DNA and containment mean that the

recombinant *A. niger* strains eligible for the tiered exemption should pose no greater risks than naturally occurring strains of *A. niger*.

(iii) *Aspergillus oryzae* is an asexual fungus found in nature and used for hundreds of years in the production of soy sauce, miso and sake without recorded incidents. This fungus has no reported adverse effects on either plants or animals. It has been suggested that genetic engineering of *A. oryzae* might inadvertently produce an aflatoxigenic strain. Naturally occurring strains of *A. oryzae* are not known to produce aflatoxins; however, some scientists believe that *A. oryzae* is a domesticated version of *A. flavus* and may possess dormant genes for aflatoxin production. It is likely that companies have already been using genetically modified strains of *A. oryzae*, but these strains have not yet met the PMN reporting requirements, that is, they are not intergeneric. The limitations placed by the tiered exemption on the introduced genetic material, in particular the well-characterized and limited in size restrictions, should reduce the likelihood that any sequences relating to aflatoxin production could be introduced. The containment requirements would limit exposure to any mycotoxins produced. In addition, *A. oryzae* does not colonize humans. In general, the restrictions placed on the introduced genetic material and containment mean that the recombinant *A. oryzae* strains eligible for the tiered exemption should pose no greater risks than naturally occurring strains of *A. oryzae*.

(iv) *Bacillus licheniformis* is an aerobic sporeforming bacterium that is well defined taxonomically. It can be readily isolated from the environment, where it persists primarily as endospores. Many strains have been tested and shown to have no adverse effects on humans, animals or plants. *B. licheniformis* has been reported as an opportunistic pathogen in livestock; however, it has never been diagnosed as a causal agent. *B. licheniformis* has a history of safe use in large-scale fermentation production of specialty chemicals and substances such as citric acid and detergent enzymes. Although the majority of experience with industrial fermentations employing *B. licheniformis* is with asporogenic strains, all strains of this microorganism are being recommended for the tiered exemption.

(v) *Bacillus subtilis* is an aerobic sporeforming bacterium which is not completely defined at either the genus or species level. This species is commonly found in nature, particularly in terrestrial environments. Many strains have been tested and shown to have no adverse effects on humans, animals or plants. Reports of *B. subtilis* acting as an opportunistic pathogen are few in number and have not been well substantiated. *B. subtilis* has a history of safe use in large-scale fermentation production of specialty chemicals and enzymes and even as a source of single cell protein for human consumption in Asia. Although the majority of experience with industrial fermentations employing *B. subtilis* is with asporogenic strains, all strains of this microorganism are being recommended for the tiered exemption.

(vi) *Clostridium acetobutylicum* is an obligate anaerobic endospore-forming bacterium which has been isolated from soils, sediments, well water, and from animal and human feces. Various strains of *C. acetobutylicum* have a history of safe use industrially or in research for the production of butanol and acetone from various feedstocks. While *C. acetobutylicum* may survive in the environment, it is not likely to cause any significant environmental effects. Although the current taxonomic classification of *Clostridium* species is not well-defined, *C. acetobutylicum* can be distinguished from closely related species which are known to be human pathogens. In general, the restrictions placed on the introduced genetic material and containment mean that the recombinant *C. acetobutylicum* strains eligible for the tiered exemption should pose not greater risks that the naturally occurring strains of *C. acetobutylicum* which have been used in industry without reports of adverse effects to workers or the environment.

(vii) *Escherichia coli* K-12 is a strain which is well defined taxonomically, although the genus Escherichia as a whole is not. *E. coli* K-12 strains can be readily distinguished from those close relatives that are pathogens. *E. coli* K-12 is a debilitated bacterium which does not normally colonize the human intestine. It has also been shown to survive poorly in the environment, has a history of safe commercial use, and is not known to have adverse effects on humans, microorganisms, or plants. Although some K-12 substrains produce low levels of toxins, toxin expression by these substrains is mitigated by *E. coli* K-12's poor survival in the environment and its inability to colonize normal human or animal hosts.

(viii) *Penicillium roqueforti* is an asexual fungus which decomposes organic materials in nature. Most strains of *P. roqueforti*, including those used in cheese production, have been shown capable of producing a variety of mycotoxins. *P. roqueforti's* long history of use in the production of blue cheese has shown no adverse effects. *P. roqueforti* is generally considered to be a benign organism, but it does raise concerns because of its ability to produce mycotoxins under certain conditions. Despite these concerns, the organism has a history of use without noted reports of adverse effects to workers or the environment. In general, the restrictions placed on the introduced genetic material and containment mean that the recombinant *P. roqueforti* strains eligible for the tiered exemption should pose no greater risk than naturally occurring strains of *P. roqueforti*.

(ix) *Saccharomyces cerevisiae* is a yeast that occurs commonly in the environment. Although it is not well defined taxonomically and survives well in the environment, it has a history of safe use in the commercial production of many products (e.g., beer). Further, it is not known to cause pathological effects on humans, plants, or animals. *S. cerevisiae* has no known effects on microorganisms, other than possible effects on strains of its own species.

(x) *Saccharomyces uvarum* is a yeast capable of fermenting a variety of sugars into ethanol. *S. uvarum* has a long history of safe use in production of alcoholic beverages and industrial ethanol. Although it is expected to survive in the environment, it is not expected to cause any adverse environmental effects. While *S. uvarum* has been used industrially for years, specific strains have not been distinguished.

b. *The introduced genetic material*. In order to qualify for either Tier I or Tier II exemption, any introduced genetic material must be limited in size, well-characterized, free of certain nucleotide sequences, and poorly mobilizable.

(i) *Limited in size*. Introduced genetic material must be limited in size to those segments required to perform the intended function, as described at proposed § 725.421(a). This criterion reduces uncertainty by excluding the introduction into a recipient of extraneous and potentially uncharacterized genetic material. The requirement that the regulatory sequences permit the expression solely of the structural gene(s) of interest reduces risk by preventing expression of genes downstream of the inserted genetic material. The limitation on the vector sequences that are components of the introduced genetic material prevents the introduction of novel traits beyond those associated with the gene(s) of interest. The overall result of the limited in size criterion is improved ability to predict the behavior of the resulting microorganism. EPA requests comment on the usefulness of this criterion in reducing uncertainty about the behavior of the new microorganism and any difficulties researchers may have in isolating the genetic material required to perform the intended functions.

(ii) *Well-characterized*. The requirement at proposed § 725.421(b) that the introduced genetic material be well-characterized also contributes to improved ability to predict the behavior of the resulting microorganism. Well characterized includes knowledge of the function of the introduced sequences and the phenotypic expression associated with the introduced genetic material. Genetic material which has been examined at the restriction map or sequence level, but for which a function or phenotypic trait has not yet been ascribed, is not considered well-characterized.

Well-characterized would include knowing whether multiple reading frames exist within the operon. This relates to whether more than one biological product might be encoded by a single sequence, and addresses the possibility that a modified microorganism could display unpredicted behavior should such multiple reading frames exist and their action not be anticipated.

(iii) *Free of certain sequences*. In addition to improving the ability to predict the behavior of the modified microorganism, the well-characterized requirement ensures that segments encoding for either part or the whole of the toxins listed at proposed § 725.421(d) would not inadvertently be introduced into the recipient microorganism (Refs. 11 and 12).

The toxins listed at proposed § 725.421(d) are polypeptides of relatively high potency. Other types of toxins (e.g., modified amino acids, heterocyclic compounds, complex polysaccharides, glycoproteins, and peptides) are not listed for two reasons. First, their toxicity falls within the range of moderate to low. Second, these types of toxins generally arise from the activity of a number of genes in several metabolic pathways (multigenic).

In order for a microorganism to produce toxins of multigenic origin, a large number of different sequences would have to be introduced and appropriately expressed. It is unlikely that all of the genetic material necessary for metabolizing multigenic toxins would be inadvertently introduced into a recipient microorganism when requirements that the genetic material be limited in size and well-characterized are followed. Should any of the necessary sequences not be introduced, or not be expressed appropriately by the recipient, a toxin of multigenic origin would not be produced. EPA, thus, sees no reason why a manufacturer who wishes to modify a microorganism listed in proposed § 725.420 with a single or a few sequences involved in metabolism of a multigenic toxin should not be allowed to do so. Introduction of a single or a few such sequences into a candidate microorganism should not result in production of a multigenic toxin and thus would not present significant risk.

Similarly, other properties that might present risk concerns result from the interactive expression of a large number of genes. For example, pathogenic behavior is the result of a large number of genes being appropriately expressed. Because of the complex nature of behaviors such as pathogenicity, the probability is low that an insert consisting of well-characterized, limited in size genetic material could transform the microorganisms listed at proposed § 725.420 into microorganisms which display pathogenic behavior. For this reason, with the exception of certain toxins which are listed because of their potency, EPA is not listing at proposed § 725.421(d) sequences that are one of a series of sequences needed in combination in order for a microorganism to display a complex behavior such as pathogenicity. If commenters believe they can identify sequences which present risk

concerns which should be addressed and listed at proposed § 725.421(d), EPA requests they inform the Agency of these sequences.

(iv) *Poorly mobilizable*. The requirement, at proposed § 725.421(c), that the introduced genetic material be poorly mobilizable reduces potential for transfer of introduced genetic sequences to other microorganisms in the environment. Such transfers would occur through the interaction of the introduced microorganism with indigenous microorganisms through conjugation, transduction, or transformation. Through such transfers, the introduced genetic material could be transferred to and propagated within different populations of microorganisms, including microorganisms which may never previously have been exposed to this genetic material. It is not possible to predict how the behavior of these potential recipient microorganisms will be affected after uptake and expression of the genetic material.

Since EPA is not limiting the type of organism that can serve as the source for the introduced genetic material, some limitation is placed on the ability of the introduced genetic material to be transferred. This limitation mitigates risk by significantly reducing the probability that the introduced genetic material would be transferred to and expressed by other microorganisms.

The transfer frequency of $10^{-8}$ was selected as defining ''poorly mobilizable'' for four reasons. First, it represents the lower end of the range of transfer frequencies observed in nature. Transfer of plasmids, for example, commonly occurs through conjugation between bacteria at rates ranging from no detectable transfer (typically less than $10^{-8}$ transfer events per donor) to $10^{-2}$ transfer events per donor in soil, water and sewage (Ref. 13). A similar range of transfer frequencies has been associated with transduction of chromosomal and plasmid DNA in soil and aquatic microcosms (Refs. 14, 15, and 16). Also, a limited number of studies on natural transformation have documented a range of transformation events from $0.3 \times 10^{-8}$ to $1 \times 10^{-8}$ transformants per recipient (Ref. 17). Second, studies of certain genetic traits (e.g., amino acid auxotrophy, resistance to antibiotics) suggest the spontaneous rate of mutation to be within the range of $10^{-5}$ to $10^{-8}$ per cell generation (Refs. 18 and 19). A frequency of $10^{-8}$ appears to represent, therefore, a baseline frequency at which change occurs in genetic material. Third, this frequency sets the technical limit for measurability. Below the rate of spontaneous mutation, it becomes difficult to distinguish gene transfer from mutation. Fourth, the $10^{-8}$ criterion should not be difficult to meet, and, in fact, is a standard employed in the NIH Guidelines.

The $10^{-8}$ frequency is attainable given current techniques. Plasmids with transfer rates of $10^{-8}$ exist or are easily constructed. In bacteria this low rate is readily engineered through the inactivation of the transfer functions of mobile genetic elements, or the inactivation/removal of pilus formation functions of plasmids (Ref. 20). Some of the plasmids most commonly employed as vectors in genetic engineering (e.g., pBR325 and pBR322) have mobilization/transfer frequencies of $10^{-8}$ or less. The plasmid pBR322 has been used as a vector to construct several microorganisms reviewed by EPA under the 1986 Policy Statement.

The criteria set for ''poorly mobilizable'' for transduction and transformation should not prevent most microorganisms from meeting the exemption criteria, since the majority of transfer frequencies reported for transduction and natural transformation are less than $10^{-8}$. Higher frequencies are likely only if the introduced genetic material has been altered or selected to enhance frequency.

Fungal gene transfer has also been considered in development of the poorly mobilizable criterion. Although mobile genetic elements such as transposons, plasmids, and double stranded RNA exist in fungi and can be readily transferred, this transfer usually is only possible between members of the same species during anastomosis, a process specific to fungi. Since anastomosis only occurs between members of the same species, the introduced genetic material would not be transferred to distantly related fungi as may occur with bacteria.

Based on suggestions made at the July 22, 1991 BSAC Subcommittee meeting, EPA proposes the following definition for ''poorly mobilizable'': ''The ability of the introduced genetic material to be transferred and mobilized is inactivated, with a resulting frequency of transfer of less than $10^{-8}$ transfer events per recipient.'' For microorganisms with introduced genetic material associated with conjugative plasmids or conjugative transposons, this criterion can be met by inactivation of transfer or mobilization functions which reduce transfer frequency. In instances where introduced genetic material is located on the chromosome, steps can be taken to insure a low transfer frequency by transduction and transformation by reducing opportunities for illegitimate recombination. EPA requests comment on the appropriateness of its definition of poorly mobilizable and whether there are alternative or additional methods for demonstrating that introduced genetic material is poorly mobilizable that should be included in the definition.

(v) *Effect of introduced genetic material criteria*. The requirements placed on the introduced genetic material, in concert with the level of safety associated with the recipient microorganisms, ensure that the resulting microorganisms present low or negligible risk. The probability is low that the insertion of genetic material meeting EPA's criteria into such microorganisms will change their behavior so that they would

acquire the potential for causing adverse effects. Risks would be mitigated by the four criteria placed on the introduced genetic material, the relative safety of the microorganisms listed at proposed § 725.420, and the inactivation criteria specified for the Tier I exemption. In the case of Tier II exemption, risks would be mitigated in light of the four criteria placed on introduced genetic material, the relative safety of the microorganisms listed at proposed § 725.420, and EPA's review of the conditions selected.

c. *Standards for minimizing the number of microorganisms emitted from the facility*. The standards prescribed for Tier I exemption require that the structure(s) be designed and operated to contain the microorganism, that access to the structure be limited to essential personnel, that inactivation procedures shown to be effective in reducing the number of viable microorganisms in liquid and solid wastes be followed prior to disposal of the wastes, that features to reduce microbial concentrations in aerosols and exhaust gases released from the structure be in place, and that general worker hygiene and protection practices be followed.

(i) *Definition of structure*. EPA considers the term ''structure'' to refer to the building or vessel which effectively surrounds and encloses the microorganism. Vessels may have a variety of forms, e.g., cubic, ovoid, cylindrical, or spherical, and may be the fermentation vessel proper or part of the downstream product separation and purification line. All would perform the function of enclosing the microorganism. In general, the material used in the construction of such structure(s) would be impermeable, resistant to corrosion and easy to clean/sterilize. Seams, joints, fittings, associated process piping, fasteners, and other similar elements would be sealed.

(ii) *Standards to minimize microbial release*. EPA is proposing, for several reasons, a somewhat cautious approach in prescribing standards for minimizing the number of microorganisms emitted through the disposal of waste and the venting of gases. First, a wide range of behaviors can be displayed by microorganisms modified consistent with EPA's standards for the introduced genetic material. Second, EPA will not conduct any review whatsoever for Tier I exemptions. EPA believes the requirement to minimize emissions will provide a measure of risk reduction necessary for making a finding of no unreasonable risk. Taken together, EPA's standards ensure that the number of microorganisms emitted from the structure is minimized.

EPA's proposed standards for minimizing emission specify that liquid and solid waste containing the microorganisms be treated to give a validated decrease in viable microbial populations so that at least 99.9999 percent of the organisms resulting from the fermentation will be killed. During normal fermentation processes, bacteria generally reach a level of $10^{10}$ to $10^{11}$ colony forming units per milliliter (Ref. 21). A simple calculation assuming no dilution of the fermentor broth and a minimum inactivation efficiency of 99.9999 percent (or a 6 log reduction) results in an estimate of the concentration of viable organisms released from the facility of at most approximately $10^5$ bacteria per milliliter. This number is likely to be lower, since the required reduction is the minimum validated inactivation and the actual kill is likely to be greater.

Fungi have greater biomass per colony forming unit and therefore are incapable of reaching the high numbers that bacteria in fermentation vats achieve. During the fermentation process, fungal populations frequently reach population densities of $10^6$ to $10^7$ microorganisms per milliliter (Ref. 21). The proposed level of inactivation would result in almost all fungi from the fermentation process being rendered nonviable. Here too, the actual reduction in number is likely to be greater that the minimum required by EPA.

Since the bacteria used in fermentation processes are usually debilitated, either intentionally or through acclimation to industrial fermentation, the small fraction of microorganisms remaining viable after inactivation treatments will likely have a reduced ability to survive during disposal or in the environment. This is because microorganisms repeatedly cultured in specific growth conditions become adapted to those conditions and often lose the ability to survive in different conditions. This is particularly true when microorganisms are used in industrial fermentations wherein most, if not all, of the microorganism's nutritional and other needs are met to ensure rapid growth and good product yield. Moreover, industrial companies, in an attempt to keep their proprietary microorganisms from competitors and to reduce the microbial numbers to those permitted by local sanitation authorities, modify the microorganisms to increase the ability of their microorganisms to survive and perform their assigned tasks in the fermentor but decrease their ability to survive in the environment external to the fermentor.

When treated wastes are placed in the sanitary sewage line during disposal, factors such as changes in pH, temperature, ionic balance, and dilution adversely affect any microorganisms remaining viable subsequent to inactivation treatment. Similarly, when such wastes are left in the form of cakes for several hours at room temperature, the lack of nutrients and sufficient suitable electron acceptors (oxygen for aerobes, other substances such as an organic compound or sulfur for anaerobes) further reduces viability. Based on these considerations, EPA believes that under its proposed standards, few viable microorganisms will be emitted from the facility

through the route of liquid and solid wastes.

EPA requirements also address microorganisms in the exhaust from the fermentor and along the production line. To address exhaust from fermentors, EPA is proposing that the number of microorganisms in fermentor gases be reduced by at least two logs prior to the gases being exhausted from the fermentor. EPA selected this number based on an estimate of the numbers of microorganisms likely to be in the exhaust from an uncontrolled fermentor and common industry practice. Several studies cited by Battelle (Ref. 22) suggest that a typical viable microorganism load in uncontrolled fermentor exhaust is about $5 \times 10^4$ organisms per cubic foot. A reduction of two logs would reduce the number to approximately $5 \times 10^2$ microorganisms per cubic foot. The actual number is likely to be lower, since the required reduction is a minimum and the number removed may be greater.

The number of microorganisms that remain viable subsequent to being exhausted from the fermentor is likely to be lower still. First, it is generally not common industry practice to run fermentors in an uncontrolled fashion. Second, microorganisms in fermentor exhausts would be within aerosols. Aerosolization is, in general, very stressful for microorganisms, because of the physical pressures associated with aerosol formation and the high probability of dehydration (Refs. 22 and 23). Moreover, microorganisms that are physiologically acclimated to the growth conditions within the fermentor are likely to be compromised in their ability to survive aerosolization. EPA anticipates, therefore, that few microorganisms will survive the stresses of aerosolization associated with being exhausted in a gas from the fermentor. The provision requiring reduction of microorganisms in fermentor exhaust gases contributes to minimizing the number of viable microorganisms emitted from the facility.

EPA requests comment on whether its standards for minimizing releases of microorganisms from facilities are appropriate for this exemption. EPA is particularly interested in whether commenters can suggest reasonable alternative methods for reducing releases from facilities and provide the rationale for these alternatives.

EPA is also proposing that the requirements specify that other systems be in place to control dissemination of microorganisms by other routes. This would include programs to control pests such as insects or rats, since these might serve as vectors for carrying microorganisms out of the fermentation facilities.

(iii) *Worker protection*. The requirement to minimize microbial emissions, in conjunction with the requirement for general worker safety and hygiene procedures, also affords a measure of protection for workers. Potential effects on workers that exist with microorganisms in general (e.g., allergenicity) will be present with the microorganisms qualifying for this exemption. As with other substances that humans may react to (e.g., pollen, chemicals, dust), the type and degree of allergenic responses is determined by the biology of the exposed individual. It is unlikely that a microorganism modified in keeping with EPA's specifications for the introduced genetic material would induce a heightened response. The general worker hygiene procedures specified by EPA should protect most individuals from the allergenic responses associated with microorganisms exhausted from fermentors and/or other substances emitted along the production line. The EPA requirement that entry be limited to essential personnel also addresses this consideration by reducing to a minimum the number of individuals exposed.

(iv) *Guidance for Tier II*. EPA is not specifying standards for minimizing the number of microorganisms emitted from the facility for microorganisms qualifying for Tier II exemption. Rather, the Agency requests that submitters utilize as guidance the standards set forth for Tier I procedures. The procedures proposed by the submitter in a Tier II exemption request will be quickly reviewed by the Agency (45 days). EPA will have the opportunity to evaluate whether the procedures the submitter intends to implement for reducing the number of organisms emitted from the facility are appropriate for that microorganism.

d. *Benefits of the tiered exemption*. Substantial benefits are associated with this proposed exemption. The recipient microorganisms are already widely employed in general commercial uses subject to TSCA reporting. These include microorganisms used to produce enzymes for detergent use or biomass conversion, and production of specific compounds such as plant or microbial growth promoting factors.

The Agency believes this exemption will result in resource savings both to EPA and industry without compromising the level of risk management afforded by the 90–day MCAN review. The microorganisms named as recipients for the tiered exemption have been assessed for risk, criteria limiting the potential for transfer of and expression of toxin sequences have been provided, and the conditions of use are specified in the exemption (Tier I) or will be reviewed by EPA (Tier II). EPA requirements for minimizing numbers of viable microorganisms emitted are within standard operating procedures for the industry, and both the procedures and the structures specified in the exemption are the type industry uses to protect their products from contamination.

The exemption will result in reduced reporting costs and a decrease in delay associated with reporting requirements. The savings in Agency resources can be directed to reviewing activities and microorganisms which present greater uncertainty.

This exemption should facilitate development and manufacturing of new products and the accumulation of useful information. When balanced by the potential resource savings and many industrial benefits of these microorganisms, the Agency finds the potential benefits of exempting uses of these microorganisms under the specific criteria will not present unreasonable risk.

EPA is considering designating other microorganisms as eligible for this exemption, dependent upon risk assessments for these microorganisms indicating that they present no unreasonable risk under the conditions of use. A list of microorganisms EPA believes are used by industry for TSCA uses appears in a support document in the docket for this rulemaking. EPA plans to evaluate many of these to determine whether they qualify as recipient microorganisms eligible for this exemption. The goal of the evaluation is to ensure that the microorganisms would present no unreasonable risk when used under the conditions of this exemption. Persons possessing information demonstrating no unreasonable risk and thus supporting eligibility for the tiered exemption for these microorganisms or other microorganisms are encouraged to submit such information to EPA to facilitate this process. As noted previously, this information could be submitted using the procedures at proposed § 725.67.

## IV. Other Issues

### *A. Microorganisms Covered in This Rulemaking*

1. *Microorganisms included*. In this proposed rule, EPA, on the advice of its BSAC, is including in its definition of ''microorganism'' those organisms classified in the kingdoms Monera (or Procaryotae), Protista, and Fungi, the Chlorophyta and the Rhodophyta of the Plantae, and viruses and virus-like particles. This definition, which uses the five kingdom classification system of Whittacker (Ref. 24), includes, but is not limited to bacteria, protozoa, fungi, mycoplasmas, mycoplasma-like organisms, spiroplasmas, microphytoplanktons, and green and red algae. Viruses and virus-like particles (e.g viroids, satellites, virusoids) are also considered to be microorganisms by EPA, even though they are classified in a unique classification system described by Francki, et al. (Ref. 25). Should new categories of organisms within the Monera, Protista, Fungi, and the Chlorophyta and the Rhodophyta of the Plantae be identified, these also would be considered microorganisms under this proposed rule. EPA requests comment on its approach to the definition of microorganisms. EPA is particularly interested in comment regarding the appropriateness of including organisms from the Chlorophyta and the Rhodophyta of the Plantae in its microorganism definition.

The organisms belonging to the Monera, Protista and Fungi are primarily unicellular. Members of the Chlorophyta and the Rhodophyta are also primarily unicellular. As members of the Thallophyta, they show little if any tissue differentiation (the entire plant is known as a thallus), the reproductive structures are often unicellular and lack a protective wall or jacket of sterile cells, and the zygotes do not form embryos within a female reproductive organ. The organisms of the Monera, Protista, Fungi, Chlorophyta, and Rhodophyta may be prokaryotes or eukaryotes, and may or may not possess cell walls.

Each type of microorganism can be significantly different, one from another. Some measure of the differences between them can be seen in the fact that the descriptor, ''microorganism'', spans four of the five kingdoms into which all organisms are classified. These differences present several challenges in constructing a rule.

2. *Inclusion of viruses and virus-like particles*. One important consideration under TSCA revolves around the approach to viruses and virus-like particles. Viruses are included by EPA in the designation ''microorganisms.'' These entities, which are among the smallest of microorganisms, differ from other microorganisms in several ways. First, they are non-cellular entities, lacking a delineating cell membrane and the metabolic machinery for the basic cellular function of energy generation. Second, they contain only one type of genetic informational molecule, either RNA (ribonucleic acid) or DNA (deoxyribonucleic acid). Third, viruses are obligate intracellular inhabitants. They cannot reproduce independently outside of a host cell. For this reason, viruses have historically been identified according to the host they infect, i.e., plant viruses reproduce in plant cells, animal viruses in animal cells, and bacterial viruses in bacterial cells. There are also viruses of fungi, algae, and protozoa. More recently a unique classification system has been developed based on the genome structure and expression, as well as on structural features of the virus particles (Ref. 25). Because their reproduction within cells can result in disruption of the host cell, viruses are generally considered to be pathogens. Viroids are virus-like particles which are also pathogens. These entities are implicated in plant diseases such as potato spindle tuber disease.

When the BSAC Subcommittee met on July 22, 1991, they considered EPA's approach to microorganisms under TSCA. They raised several issues with regard to viruses and virus-like particles. They noted that viruses are by definition pathogens. As viruses in general have smaller genomes than other microorganisms and a greater percentage of the genome is related to pathogenicity, a change in the viral genome is more likely to affect pathogenicity than a change in the genome of microorganisms such as bacteria and fungi. Even when a change occurs solely within a single genome, viruses and virus-like particles may warrant a more

cautious approach than other microorganisms. Finally, plant and animal viruses are known to shift host range under *in vitro* tissue culture conditions, other unique conditions, or in non-traditional hosts, and this, in and of itself, is an important risk consideration.

Thus, viruses and virus-like particles, because of their unique characteristics, present different issues than other microorganisms. This is particularly true of the viruses that attack macroorganisms (humans, animals, and plants); and the use of these viruses probably warrants scrutiny regardless of whether the virus is new or existing.

Viruses that infect other microorganisms (e.g., the viruses of protozoa, fungi, and bacteria), may present a somewhat different risk picture from those that infect macroorganisms. Although it appears theoretically possible for a virus of a microorganism (also termed a phage) to permanently eliminate its host microorganism from a habitat, studies done to date do not provide strong evidence that this occurs (Ref. 24), possibly because microorganisms are capable of rapidly developing resistance to phage infection. Phage infections appear rather to result in a temporary fluctuation rather than a permanent change in the numbers of a microorganism in a specific habitat. Moreover, redundancy in function found in natural microbial communities (i.e., many species are capable of performing the same ecological function (Ref. 5)) may cushion the effects of these population fluxes.

To address viruses for this rulemaking, EPA has distinguished between those that infect microorganisms and those that infect macroorganisms. Phages will be considered MGEs and the MGE guidance discussed in Unit I.C. of this preamble will apply to them. Therefore, a phage which has been modified to contain genetic material from a second phage whose host microorganism is in a different genus than the modified phage would be considered a ''new'' microorganism subject to TSCA section 5 reporting. Similarly, a phage modified to contain genetic material from an organism classified in a different genus than the genus from which the modified (recipient) phage was isolated would be considered intergeneric. Under this interpretation, a phage which has been modified to contain genetic material from a virus of a macroorganism would also be considered a ''new'' microorganism.

With regard to viruses of macroorganisms, EPA believes that certain viruses of macroorganisms would be subject to TSCA jurisdiction if they were employed in TSCA uses. As discussed in Unit I.C. of this preamble, certain product uses are excluded from coverage under TSCA, the most notable for viruses being the exclusions for pesticides (but not pesticide intermediates) which are covered under FIFRA and for food, drugs, cosmetics, and their intermediates, which are covered by FFDCA. While other uses could potentially be subject to TSCA, EPA has not at this time been able to identify viruses of macroorganisms in uses that might be subject to TSCA. EPA requests comments on whether there are known uses of viruses of macroorganisms that would be subject to TSCA and whether an intergeneric approach such as that used for phages would be appropriate for the viruses of macroorganisms. Comment is also requested on whether EPA's approach for oversight of phages under TSCA section 5 is appropriate.

*B. Listing Microorganisms on the Inventory*

This Unit describes how EPA proposes to explicitly list microorganisms on the TSCA Inventory after MCAN review and the rationale for the proposed listing.

1. *The components of explicit listing*. EPA proposes to identify microorganisms on the Inventory using a taxonomic designation and a consistent set of supplemental information on phenotypic and genotypic traits necessary to identify the microorganism as precisely as possible. EPA expects that this information would be a portion of the information included in MCAN submissions.

a. *Taxonomic designation*. The taxonomic designations to the strain level, as appropriate, would be provided for the recipient microorganism and the donor(s) of the introduced genetic material. Taxonomic designations may be those assigned by individual submitters or by a culture collection. The designations would be substantiated by a letter from a culture collection verifying the designation, by literature references, or by the results of tests conducted for the purpose of taxonomic classification. Upon request, the data supporting the taxonomic designation should be provided to EPA. Where possible, the genetic history of the recipient microorganism should be documented back to the isolate from which it was derived.

b. *Supplemental information*. Many taxonomic designations at the species level define phenotypically and genotypically diverse groups of microorganisms. Therefore, supplemental information will be used to identify as precisely as possible a specific microorganism on the Inventory. Information on phenotypic and genotypic traits is necessary only to the extent that it assists in the specific identification of the reported microorganism.

(i) *Phenotypic traits*. This information concerns the characteristics that reflect the interaction of a microorganism's genotype and the environment in which it is intended to be used. For example, information on intentionally added biochemical and physiological traits is pertinent, since these traits may affect the behavior and fate of a microorganism in the environment. Where possible, submitters should prioritize phenotypic traits in order of those likely to significantly change the microorganism's behavior and

thus its potential risk. Such important phenotypic changes may include a change from asporogeny to spore-forming, an increase in the amount of a specific product for which the microorganism is being used as an intermediate, or the activation of a previously inactive enzyme that is known to have negative human health or ecological effects.

(ii) *Genotypic traits*. This information concerns the distinguishing genotypic characteristics of a microorganism, including the identity of the genetic material that is introduced into the recipient microorganism and the methods used to construct the reported microorganism. For example, information on the vector construct, cellular location, and number of copies of the introduced genetic material is pertinent, since the vector may add genetic material and traits, and the microorganism's phenotypic traits may be affected by the number of copies and location of the introduced genetic material.

c. *Deposit in a culture collection*. Because microorganisms are complex substances and because of the nature of the differences that will be used to distinguish between similar organisms (isolates), EPA is considering requiring that microorganisms listed on the Inventory be deposited in a recognized culture collection. Deposited microorganisms could serve as references for determining whether a related, unreported microorganism, or a subsequently modified, inventoried microorganism is the same as one already listed on the Inventory. Comments on this proposal and alternative suggestions of how to distinguish among closely related microorganisms are requested.

2. *Inventory status of similar and subsequently modified microorganisms*. Since publication of the 1986 Policy Statement, EPA has reviewed several intergeneric microorganism PMNs for general commercial use. As discussed previously, the Agency has received an NOC for most of these microorganisms, and these are listed on the TSCA Inventory. The Agency recognizes that subsequent to listing a microorganism on the Inventory, original submitters may make modifications to the genetic material of the inventoried microorganism or companies other than the original submitter may construct microorganisms which may be equivalent to inventoried microorganisms. Questions would arise as to whether the modified microorganism is equivalent to the microorganism listed on the Inventory. At this time, EPA has concluded that no *a priori* guidance can be given for determining whether a similar strain will be equivalent to one listed on the Inventory. Manufacturers, producers, or importers should consult with EPA concerning the status of their microorganisms, as discussed in Unit II.B.1. of this preamble.

In making its decision on an individual microorganism, EPA will consider the phenotype of the inventoried microorganism and assess how the subsequent modifications will affect that phenotype. For example, EPA believes that a MCAN may not be required when an inventoried microorganism has undergone certain subsequent modifications of genetic material where these modifications would not be likely to significantly change the microorganism's behavior. The BSAC Subcommittee which met on July 22, 1991, suggested that EPA continue to make these decisions on a case-by-case basis, at least until EPA gains more experience. Although EPA will make its decisions on a case-by-case basis, microorganisms that may be judged by EPA to be equivalent to inventoried microorganisms include those that have experienced deletions, rearrangements, amplifications, point mutations, and/or plasmid loss within a single genome, either spontaneously or through use of chemical or physical mutagens. The Agency recognizes that deletions, rearrangements, amplifications, point mutations, and plasmid loss could occur spontaneously in any microorganism maintained in pure culture, in response to stresses such as freezing or thawing, or as a result of mistakes made during the microorganism's replication of its genetic material.

EPA recommends that potential submitters consult the Agency for clarification of their reporting obligations whenever additional changes are made to inventoried microorganisms. The Agency has reviewed several *bona fide* submissions and has determined on a case-by-case basis that the microorganisms described were equivalent to previous PMN submissions. In one case, the microorganism which was the subject of the *bona fide* submission was derived from the same strain as the inventoried microorganism using similar methods, and intrageneric material encoding the same enzyme function was introduced. Although a small number of base pairs in the intrageneric material had been genetically altered, no new trait was introduced into the *bona fide* microorganism compared to the inventoried microorganism. In a separate case, the *bona fide* microorganism contained genetically modified intrageneric material encoding the same function introduced into the inventoried microorganism as well as a small fragment of non-coding, non-regulatory intergeneric genetic material that had been derived from the same source as that introduced into the inventoried microorganism. Although a small number of base pairs had been altered in this intergeneric material, no new trait was present in the *bona fide* microorganism compared to the inventoried microorganism.

3. *Identification of microorganisms currently listed on the Inventory*. EPA wishes to provide manufacturers and processors who are using microorganisms which were listed on the Inventory prior to the 1986 Policy

Statement the opportunity to provide information for a specific, explicit listing, if necessary. In 1978, when EPA compiled its initial TSCA Inventory, 192 microorganisms were reported. These microorganisms are currently described on the Inventory by taxonomic designations only, without any supplemental information describing how they were made. They are listed in the 1985 Edition, Volume V, of the TSCA Inventory. The list of microorganisms is included in the docket for this rulemaking. The list may be obtained upon request at the address included in the FOR FURTHER INFORMATION CONTACT section of this preamble. EPA believes that most, if not all, of the 192 microorganisms would not be considered new under this proposed rule, since the listings appear to describe microorganisms which are not intergeneric. Thus, these microorganisms would be implicitly included on the Inventory and may continue to be manufactured for general commercial use.

However, EPA wishes to ensure that all listed microorganisms are described in a consistent manner. Accordingly, EPA advises manufacturers and importers of any of the 192 listed microorganisms to inform EPA of their status under this proposed rule during the public comment period. Any manufacturers of microorganisms that would be considered new under any final rules will be given the opportunity to provide information to EPA to ensure consistent listing of the microorganisms on the Inventory. If EPA is not notified about a microorganism, the Agency will assume it would be implicitly included because it is not intergeneric, and it will be removed from the Inventory list as an explicit listing under EPA's TSCA section 8(b) authority.

As discussed previously, EPA has reviewed a number of intergeneric microorganism PMNs under the 1986 Policy Statement and has listed the microorganisms on the Inventory. These microorganisms will be retained on the Inventory if the proposal becomes final. If changes are made which require alteration of Inventory listings, EPA will announce them in the **Federal Register**.

*C. SNUR Process*

EPA is not proposing any significant new use rules (SNURs) in this document. Instead, EPA is proposing, in subpart L of part 725, procedures to enable it to issue SNURs in the future. Microorganisms subject to SNUR reporting would be listed in proposed subpart M of part 725. This Unit discusses the SNUR process that EPA is proposing. This process is adapted from the process in place for traditional chemicals in part 721 with only slight modifications.

1. *SNURs applied to microorganisms.* Although EPA is not proposing SNURs for any microorganisms in this document, it is conceivable that, in the future, certain specific uses of microorganisms may raise concerns for human health or the environment. Because the behavior of a specific microorganism is influenced by the environment into which it is introduced (Refs. 5, 7, 8, and 9), it may be necessary to evaluate the risk of some microorganisms when the environment of use is changed. For example, EPA was asked whether any uses of ''Ice +'' strains of *Pseudomonas syringae* might be subject to SNUR reporting. At the time, the ''Ice +'' microorganism was being used for snowmaking at ski resorts. In that situation, EPA decided that terrestrial uses of the microorganism for such activities as snowmaking at ski resorts, icemaking at ice skating rinks, commercial air conditioning, and spray-ice construction applications did not pose significantly different exposures and therefore would not require SNUR reporting to EPA. However, EPA did indicate that because use of the microorganism for cloudseeding would present a significantly different exposure scenario than the terrestrial uses, EPA might require SNUR reporting prior to use of the live microorganism for cloudseeding. In such cases, EPA believes it may be appropriate to use SNUR authority to monitor the commercial development of these substances so that EPA can be apprised of significant increases in exposure potential or significant changes in exposure patterns. These significant increases may warrant control measures or testing. As noted earlier, the MCAN submission and review process will be used for microorganisms subject to SNUR reporting.

2. *Expedited process for issuing SNURs.* If EPA finds it necessary to issue SNURs for new microorganisms reviewed under the MCAN process, EPA will use, when appropriate, expedited procedures based on those established in part 721, subpart D. The procedures for issuing expedited SNURs for microorganisms are set forth in proposed § 725.980. EPA is not soliciting separate public comment on these procedures, since they have already been adopted by EPA. This section relies on the rationale originally stated in the **Federal Register** notices establishing the expedited SNUR process for other new substances under part 721. The SNUR procedures are discussed here and included in the regulatory text for completeness, so that the public will understand all the regulatory provisions potentially applicable to microorganisms.

A limited amount of toxicity data is typically submitted with premanufacture notifications (PMNs) for chemical substances. Thus, EPA often bases its reviews on structure-activity relationships (SARs). MCANs are expected to present similar problems in data gaps, since current knowledge of microbial ecology is limited, and microorganisms subject to TSCA are expected to be used in an ever-expanding variety of applications and thus a multitude of different

exposures. Should the Agency determine it does not possess sufficient information to make a risk judgement, EPA could find under TSCA section 5(e) that it had insufficient information to determine whether the new microorganism presents an unreasonable risk of injury to health or the environment. In most such cases, EPA believes that it is appropriate to negotiate a consent order under section 5(e) with the notice submitter to control human exposure and/or environmental releases until test data or other information sufficient to assess adequately the potential hazard become available. Current experience indicates that section 5(e) consent orders for traditional chemicals have specified a variety of control measures. For microorganisms, EPA may place restrictions on site location or size, production volume or method of application, field or laboratory containment procedures, routine or emergency mitigation procedures, or testing procedures.

Section 5(e) orders are binding on the original notice submitter but do not apply to other manufacturers of the same microorganism. Without additional regulation, other persons can manufacture, import, or process the microorganism without EPA review and without the restrictions imposed on the original MCAN submitter by the section 5(e) order. To limit all manufacturers equally, EPA imposes SNURs.

Currently, EPA uses its SNUR authority to extend limitations in section 5(e) orders to other manufacturers, importers, and processors of chemical substances. This ensures that the original submitter and subsequent manufacturers, importers, and processors are treated in an equivalent manner. SNURs are framed so that noncompliance with the control measures or other restrictions is defined as a ''significant new use.'' Thus, other manufacturers, importers, and processors of the substances must either observe the SNUR restrictions or submit a notice to EPA at least 90 days before initiating activities that deviate from these restrictions. After receiving and reviewing such a notice, EPA would have the option of either permitting the new use or acting under section 5(e) or (f) to regulate the new submitter's activities. EPA intends to use this same process for microorganisms. In addition to assuring that all manufacturers, importers, and processors are subject to similar reporting requirements and restrictions, expedited SNURs assure that EPA would have an opportunity to review and evaluate data and, when necessary, regulate prospective manufacturers, importers, or processors of a listed microorganism before a significant new use of that microorganism occurs.

*D. Confidential Business Information*

EPA's confidential business information (CBI) policy is designed to provide effective public participation by making meaningful information available. In developing confidentiality provisions for submissions, EPA has balanced the need to provide nonconfidential information to the public in a reasonable period of time, to obtain the information it needs to respond to FOIA requests, and to allow persons to assert CBI claims with the minimum burden. In developing its position for this rulemaking, EPA has considered its experience reviewing PMNs for traditional chemicals and microorganisms and comments received on its February 1989 FR notice. This Unit discusses the requirements proposed in subpart C of part 725 and the rationale for EPA's proposal.

1. *Assertion of CBI claims*. A person may assert a claim of confidentiality for any information submitted to EPA, with certain exceptions. However, submitters are encouraged to minimize the amount of CBI in biotechnology submissions, so that the public may participate as fully as possible in the review process. All CBI claims must be asserted at the time of submission of the information.

2. *Generic information*. Submitters who claim microorganism identity and/or use as CBI also must provide generic information for release to the public. By requiring generic identity and use information, EPA would meet its obligation to provide the public with important information related to the potential risks of new microorganisms without revealing CBI. EPA needs this information to prepare **Federal Register** notices to announce EPA's receipt of submissions or EPA's decisions regarding exemption requests.

The generic designations must reveal the identity and use of the microorganism to the maximum extent possible without revealing proprietary information. Submitters are encouraged to review EPA's ''Guidelines for the Preparation of Generic Descriptions of Confidential Microorganism Identity and Use'' and consult with EPA regarding appropriate generic information prior to submitting a notice. The guidelines are available from EPA's Environmental Assistance Division (see FOR FURTHER INFORMATION CONTACT Unit). Microorganism identity must be specific enough to allow clear interpretation of any accompanying health and safety data. When the location of the release site is claimed as CBI, a generic description for use must include information regarding the type of environment into which the microorganism will be released.

3. *Identity in health and safety studies*. TSCA section 14(b) states that EPA is not prohibited from disclosing health and safety studies of substances for which TSCA section 5 notification is required, unless disclosure reveals confidential information on process or mixture. Historically, the Agency has considered specific chemical identity to be part of a health and safety study, even when it does not appear in the study. However, during the development of the PMN rule, industry expressed substantial

concern about the harm of disclosing confidential chemical identities. At that time EPA explored ways of limiting the commercial harm of such disclosure while still meeting the requirements of TSCA section 14(b) and providing the public with adequate information about health and safety studies. The CBI requirements in the final PMN rule reflected EPA's desire to balance these needs (48 FR 21722, May 13, 1983).

EPA has determined that the regulations developed to address chemical identity in health and safety studies can also be applied to microorganism identity. In this regard, if any health and safety information has been submitted for the microorganism in question, the specific microorganism identity will be held confidential only if disclosure would reveal confidential process or mixture information or if the specific microorganism identity is not necessary to interpret any of the information.

Under this approach, companies that claim specific microorganism identity confidential in their submissions and wish to argue that knowledge of the specific identity is not necessary to interpret their health and safety information are encouraged to choose generic names which are sufficiently specific to allow interpretation of such information. Sufficiently specific generic names will tend to support arguments that disclosure of the specific microorganism identity is not necessary to understand the health and safety information.

4. *Current policy for substantiation of CBI claims*. EPA currently requires submitters of all PMNs for new microorganisms to be released to the environment to substantiate confidentiality claims at the time of submission. This includes PMNs for environmental releases of new microorganisms for R&D as well as for general commercial use, but it does not require upfront substantiation of CBI claims in PMNs for closed system uses of new microorganisms. This policy will continue in effect, until a final rule is promulgated for microorganisms. Like the chemicals program, EPA requires that CBI claims in NOCs for microorganisms be reasserted and resubstantiated when the NOC is submitted.

5. *Proposed changes for substantiation of CBI claims*—a. *Submissions for general commercial uses of microorganisms*. To balance the competing needs of opening the review of submissions for microorganisms to public scrutiny and participation while protecting legitimate CBI claims, EPA proposes to require upfront substantiation of CBI claims in all submissions for general commercial uses of microorganisms. EPA will not distinguish between closed system uses and other uses of microorganisms. Anyone submitting a MCAN, a TME, or a Tier II exemption request will be required to substantiate CBI claims at the time of submission. Failure to include substantiation of any CBI claims, by submitting written answers to the questions, will render the submission incomplete; and it will be returned to the submitter.

EPA believes that the upfront substantiation requirement for CBI claims will impose little burden on submitters of MCANs, TMEs, and Tier II exemption requests. Because MCAN, TME, and Tier II exemption request submitters are ready to put their products on the market, they should be able to justify why it will continue to be necessary to keep certain information confidential. In addition, given the shorter review period for TMEs and Tier II exemption requests, sufficient information may not be made available to the public if upfront substantiation of CBI claims is not required.

b. *TERA submission*. With respect to upfront substantiation for TERAs, EPA is proposing two options and asking for public comments on both. In comments in response to the 1989 FR notice, industry groups raised the issue of adequate protection for R&D. Pointing out that R&D activities involving microorganisms will be facing regulatory burdens that are not imposed on chemical R&D, industry groups said that additional burdens combined with insufficient CBI protection at the R&D stage could reduce incentives to innovate. While submitters are particularly concerned about protecting information at the R&D stage, the public is most interested in participating in the reviews of the first environmental releases of new microorganisms. Public interest groups commented that upfront substantiation is essential to allow public access to information in time to participate in reviews. Because EPA recognizes the importance of the interests of both parties, EPA is asking for additional comments on how best to resolve this issue for CBI claims in TERAs.

(i) *Option 1: Require upfront substantiation of all CBI claims in TERAs*. EPA is aware that industry believes that this requirement imposes a greater burden on R&D submitters than is necessary. Experience gained by continuing to require upfront substantiation of CBI claims in submissions for R&D activities will help EPA determine whether this requirement improves public access to information. In the meantime, EPA specifically requests comment on how the burden to submitters could be minimized if upfront substantiation of CBI claims in TERAs is promulgated as part of the final rule.

(ii) *Option 2: Do not require upfront substantiation of CBI claims in TERAs*. The second option is to adopt the current requirements for chemical PMNs, that is, require CBI substantiation only after the receipt of a FOIA request. EPA is concerned that given the shorter review period for TERAs, insufficient information may be made available to the public if upfront substantiation of CBI claims is not required. For this reason, EPA specifically requests comment on how public access to

information could be improved if submitters were not required to provide upfront substantiation of CBI claims in TERAs.

c. *Substantiation questions*. EPA's general procedures for processing and reviewing confidentiality claims are published at 40 CFR part 2. The basic points that should be covered in CBI substantiation are set out at 40 CFR § 2.204(e)(4)(i) through (ix). To ensure that substantiation responses are appropriate for submissions involving microorganisms, EPA has developed a more specific set of questions based on the points in 40 CFR part 2. These questions, which are delineated in proposed § 725.94, are designed to reduce the burden of substantiation by focussing the inquiry on points relevant to a biotechnology product.

*E. User Fees*

Section 26(b) of TSCA provides that EPA may by rule establish fees for persons required to submit data under section 4 or 5 to defray the costs of administering TSCA. EPA must take into account the submitter's ability to pay the fee and the cost of reviewing the submitted data. EPA is using this authority to collect fees for notices submitted on microorganisms.

EPA regulations already require persons to remit fees to EPA when a PMN or SNUN is submitted to the Agency for review (40 CFR § 700.45). For MCAN submissions, EPA is proposing to amend part 700 to establish a fee of $100 for notifications submitted by small businesses, and $2,500 for all other businesses. For purposes of this proposed rule, small businesses are defined as companies with total annual sales of less than $40 million. These proposed fees for MCANs are the same as those set for submissions of PMNs for other chemical substances. EPA believes that its costs of reviewing MCAN notifications will equal or exceed the cost of reviewing PMNs for other chemical substances.

EPA is not proposing user fees for other submissions under this proposed rule, including TERAs and Tier II exemption requests. EPA is not reopening the general issues applicable to the adoption of user fees for comment in this document, since comments on the subject were addressed in a final rule published in the **Federal Register** of August 17, 1988 (53 FR 31248).

*F. Section 8(e) Reporting Requirements*

Any person who manufactures, imports, processes, or distributes in commerce a TSCA-covered microorganism, whether new or existing, and/or product(s) therefrom (including a person engaged solely in R&D) is reminded about the statutory responsibility to immediately report to EPA any information the person obtains which reasonably supports the conclusion that such microorganism, or a product therefrom, presents a substantial risk of injury to health or the environment, unless the person has actual knowledge that EPA has been adequately informed already about the information. Guidance regarding the section 8(e) reporting requirement is provided in EPA's section 8(e) policy statement (''Statement of Interpretation and Enforcement Policy; Notification of Substantial Risk'' 43 FR 11110; March 16, 1978) and its technical amendment (52 FR 20083; May 29, 1987). Additional information regarding TSCA section 8(e) reporting is provided in 56 FR 4128 (February 1, 1991); 56 FR 19514 (April 26, 1991); 56 FR 28458 (June 20, 1991); and 56 FR 49478 (September 30, 1991).

Should EPA receive a section 8(e) substantial risk notice with respect to the manufacture, importation, processing or distribution in commerce of a microorganism, EPA may proceed to regulate the activity causing the risk. If EPA determines, under authority of TSCA section 7, that the activity or microorganism, including its parts or products, on which a section 8(e) notice was received, is ''imminently hazardous'' to health or the environment, EPA may require immediate suspension of manufacturing, processing or distribution in commerce of the imminently hazardous microorganism. EPA also may require any remediation necessary to obtain permanent relief as may be necessary to protect health or the environment from the unreasonable risks associated with the microorganism. This authority applies to any ''imminently hazardous'' microorganism or its parts or products, regardless of whether the microorganism is used for R&D or manufactured for general commercial use.

The term ''imminently hazardous chemical substance or mixture'' in TSCA section 7 means a chemical substance or mixture which presents an imminent and unreasonable risk of serious or widespread injury to health or the environment. Such a risk is considered imminent if the manufacture, processing, distribution in commerce, use or disposal of the substance is likely to result in such injury before a final rule can be issued under TSCA section 6.

*G. Export Notification and State Preemption*

This Unit discusses two other provisions of TSCA concerning export notification and Federal preemption that may be of some concern to the public in implementing this proposed rule.

1. *General.* Section 12 of TSCA generally provides that the Act does not apply to chemical substances produced for export. However, section 12(b)(2) requires, in pertinent part, that EPA must be notified about the export of any substance in U.S. production that is subject to a rule, an order, or some other relief granted under section 5. EPA must then notify the government of the receiving country. EPA's export notification regulations are codified at 40 CFR part 707.

Section 18(a) provides that TSCA generally does not preempt the authority of any State or local government to regulate a chemical

substance. There are some exceptions, however. In particular, section 18(b) states that, if EPA issues a rule or order under section 5 ''which is applicable to a chemical substance'' and ''which is designed to protect against a risk of injury...associated with such substance'', no State or local government may issue or continue in effect any requirement designed to protect against the same risk, with certain exceptions. The exceptions are that the State or local requirement may be identical to the Federal requirement, may be issued under authority of another Federal law, or may prohibit use of the substance (other than in the manufacture or processing of another chemical substance or mixture).

2. *Applicability*. EPA interprets the exemption of section 12(a) to apply only to those microorganisms manufactured, processed, or distributed solely for export. If the microorganism is manufactured, processed, or distributed for any use in the United States, it is subject to TSCA (see TSCA section 12(a)(1)(A)). Thus, any R&D in the U.S. is subject to applicable regulations, as are any other activities involving a microorganism that are described in this proposed rule. Similarly, any release of microorganisms to the environment prior to export will not be considered solely for export and is therefore subject to applicable regulations.

Since the rules proposed in this document are either of general applicability and largely procedural, or are exemptions from regulation and only establish procedures to screen against potential risk, neither section 12(b) export notification nor section 18(b) preemption applies at this time.

Sections 12(b) and 18(b) would apply should EPA decide to take regulatory action against a microorganism or class of microorganisms, for example, by issuing an order under TSCA section 5(e). In such cases, section 12(b) export notification would apply automatically. While preemption under section 18(b) would apply by operation of statute, in individual cases EPA could issue rules that specifically require compliance with applicable State or local requirements.

*H. Regulatory Text Overview*

The regulatory text comprises the language which EPA is proposing to incorporate into the Code of Federal Regulations (CFR). While the preamble to this proposed rule provides the rationale for EPA's preferred approach towards the oversight of certain activities involving new microorganisms, the regulatory text includes all the proposed requirements to which the regulated community would be subject.

The regulatory text amends existing regulations regarding the collection of fees from submitters of notices under section 5 of TSCA (40 CFR part 700), to reflect the fee structure for the notices and applications that have been developed by this proposed rule. Additional amendments to parts 720, 721, and 723 consolidate TSCA section 5 review of microorganisms into part 725.

EPA is proposing to establish a new part 725 of Title 40 of the CFR. EPA believes that consolidating all requirements and procedures applicable to new microorganisms into one part of the CFR is justified because of the differences between microorganisms and other chemical substances.

The consolidation will benefit the public by providing greater clarity. Part 725 is devoted exclusively to the review of microorganisms under section 5 of TSCA and is currently divided into eight subparts. Subparts A, B, and C consolidate provisions primarily adapted from parts 720 and 721. Subpart A, which includes definitions that are applicable throughout part 725, describes general provisions and applicability. Subpart B describes administrative procedures that are applicable to all submissions under part 725. Subpart C describes confidentiality provisions that are applicable to all submissions under part 725.

Subpart D, which combines the general PMN and SNUN requirements adapted from parts 720 and 721, describes the reporting requirements and review process pertaining to MCANs. Subparts E, F, and G describe the reporting requirements and review processes for applications for exemptions from full MCAN reporting. Subpart E, which is almost entirely new, describes who is eligible to submit a TERA or receive a TERA list exemption, and what criteria must be met to receive an exemption from EPA review for certain types of R&D activities. Subpart F, which is an adaptation of § 720.38, describes the requirements for a test marketing exemption for microorganisms. Subpart G, which is entirely new, describes what criteria must be met in order to qualify for Tier I or Tier II exemptions for certain microorganisms in general commercial use. Subpart L, which is adapted from part 721, describes additional procedures for reporting significant new uses of microorganisms. Although significant new use rules are not being proposed at this time, it is intended that subpart M will list microorganisms and specific significant new uses when they are promulgated.

*I. Rulemaking Process and Public Hearings*

EPA is conducting this rulemaking under notice and comment rulemaking procedures. Interested persons have the opportunity to submit written comments to the address identified under the ADDRESSES Unit of this preamble. EPA will carefully consider all such comments.

EPA is also providing an opportunity for an informal public hearing on the proposed rule. This hearing will be held only if EPA receives a timely written request for such a hearing.

As a general matter, EPA is not required to hold a public hearing in

informal notice and comment rulemaking of this type. However, use of section 5(h)(4) modifies the general rulemaking requirements by referencing TSCA section 6(c)(2) and (3) rulemaking procedures. Under those procedures, EPA must hold an informal public hearing, if requested, and, if properly requested and granted by EPA, allow an opportunity to present rebuttal submissions and conduct cross-examinations related to disputed issues of material fact.

EPA does not anticipate that, even if a hearing is held, there will be a need for rebuttal submissions and crossexamination, because the section 5(h)(4) portion of this proposed rulemaking is based primarily on matters of science policy that do not yield disputed factual issues.

## V. Economic Impact and Regulatory Flexibility Analysis

### *A. Regulatory Impact Analysis*

1. *Introduction*. EPA has prepared a Regulatory Impact Analysis (RIA) assessing the costs, benefits, and associated impacts of regulating new microorganisms under TSCA as set forth in the proposed rule. Though direct regulatory costs attributable to the proposed rule were not estimated to be in excess of $100 million annually, EPA has designated the rule as ''significant'' under Executive Order 12866 because it raises novel policy issues arising out of legal mandates. This unit presents a summary of the RIA's key findings and estimates.

2. *Characteristics of the regulated community*. Although unable to quantify the exact magnitude of activity in biotechnology sectors affected by this rulemaking, the Agency believes that activities involving microorganisms falling within the scope of the proposed rule comprise a modest share of overall activity. EPA estimates that approximately 130 firms may be involved in commercial R&D or in general commercial use of potentially regulated microorganisms. In terms of revenue, the potentially affected universe appears to be divided sharply between large and small firms. EPA estimates roughly one-half of the companies potentially affected to have annual sales of $40 million or more, while most of those remaining are estimated to have sales under $10 million. For many of these firms, however, revenue generated from activities subject to this proposal is believed to represent only a small portion of reported sales. EPA also estimates that approximately 300 universities could be affected by the rulemaking.

3. *Costs to potential submitters*. Due to data limitations and the uncertainties associated with projecting future product development activities in biotechnology application areas subject to the proposed rule, EPA's estimates of the costs of compliance associated with this rulemaking action have been only partially quantified. In cases where the Agency was able to generate quantified estimates of compliance costs, information which would have permitted the development of more accurate estimates was frequently unavailable. In such cases, the best available information was used. Estimates are believed to represent a reasonable approximation of actual costs attributable to the rule.

In assessing the potential cost impact of the proposed rule, EPA focussed on two impact years, the first and fifth years following the time of proposal (assumed to be 1992 and 1996, for the purposes of analysis). This approach was used because of the relative immaturity of the biotechnology sectors potentially subject to the proposed rule and the difficulty in attempting to forecast long-term technological and marketing developments. However, EPA wishes to emphasize that estimated costs could be significantly higher in the long-term, owing to industry growth.

Four major cost areas were identified, based on an analysis of the requirements of the proposed rule. These areas were costs incurred in preparing various types of notification submissions or documentation; costs incurred in complying with any post review requirements for monitoring or controls that may be imposed by EPA as a result of risk concerns and uncertainties; costs incurred in substantiating confidential business information (CBI) claims; and one-time costs attributable to rule familiarization.

Incremental costs to industry (industry-wide costs excluding requirements under current policy) were estimated to fall between $890,000 and $2.2 million in year 1 and between $56,000 and $460,000 in year 5. Year 5 costs account for rule familiarization only in the case of new firms entering the affected market areas, and therefore are much less than year 1 costs, where rule familiarization costs were summed over all affected entities.

Cost impacts on individual products will vary, depending on application area. Submitters qualifying for exemptions in connection with microorganisms intended for general commercial use will realize net savings relative to current reporting requirements. On the other hand, submitters reporting R&D activities involving environmental release may realize an increase in regulatory burden under the proposed rule.

4. *Costs to the Federal government*. EPA estimated the potential costs to government associated with the proposed rule. These costs arise in connection with the Agency's processing of individual notification submissions. In estimating government cost impacts, EPA included costs estimated to be incurred in reviewing each submission. EPA professionals and members of the Biotechnology Science Advisory Committee were assumed to be involved in such review. In the event that post-review restrictions would be placed on a specific activity, such as monitoring during a field test, additional costs

attributable to the drawing up of regulatory documentation would be incurred.

Incremental costs to the government were estimated to fall between $115,000 and $122,000 in year 1, while a net savings to EPA, estimated to fall between $39,000 and $184,000, is expected in year 5. These savings arise in connection with the substantial number of full reviews that will be avoided if the exemption provisions of the proposed rule are promulgated.

5. *Benefits of the proposed rule*. EPA's regulation of new microorganisms under TSCA provides benefits to society through reduction of the potential for adverse impacts on health and the environment resulting from the use of such microorganisms. This benefit is achieved by screening new microorganisms and, when appropriate, imposing controls on microorganism use to protect society from costly and possibly irreversible damages.

For microorganisms in general commercial use, risk reduction attributable strictly to the notification requirements of proposed rule would be marginal, as these requirements are based on current policy. However, the proposed rule enhances and contributes to the overall risk reduction potential of the Agency's program under TSCA by providing for a more efficient regulatory strategy relative to current policy, focussing society's resources on those new microorganisms of greatest concern.

For microorganisms in commercial R&D, a greater proportion of overall risk reduction can be attributed to the proposed rule, since reporting in connection with field experiments has been voluntary since 1986. Although the Agency has been receiving voluntary submissions, EPA is not certain whether this practice is universal or whether those filing voluntarily would continue to do so in the absence of this proposed rule.

Over the long-term, regulation is also likely to encourage development of additional information concerning fate and effects of new microorganisms, to encourage the development of microorganisms which pose low concern for effects on human health and the environment, and to encourage public input into decisions concerning the use of new microorganisms.

Benefits may also be realized through the proposed rule's potential impact on the pace of product development. A more certain regulatory climate could stimulate business activity, as could a more reassured public. The proposed rule may also reduce the possibility of continued regulatory activity at the State and local level. A national system of potentially uncoordinated rulemaking initiatives could lead to market distortion and could hamper competition.

6. *Effects of the proposed rule on innovative activity*. As a result of the proposed rule, members of the regulated community may find product development strategies in connection with certain products to require reassessment. Since impacts of this nature could influence the degree of emphasis a firm places on innovative activity, the potential for innovation impacts was investigated.

Though great uncertainty regarding regulatory costs and the potential for a particular product's commercial success make it impossible to estimate innovation impacts quantitatively, the effects of added regulatory costs and delays on a product's lifetime cash-flow was examined. More specifically, a number of plausible product development scenarios were modeled incorporating assumptions regarding expenditures and returns over the course of a product's useful life from research to obsolescence. Regulatory burdens were then factored into the models, and profit impacts observed. Impacts realized when total regulatory costs were assumed to reach the upper-bound of EPA's estimated range could result in severe profit reductions in some cases. However, in general, EPA's analysis indicated that impacts should not be prohibitive, particularly when incremental costs are considered. Factors such as length of delay related to regulatory review, return rate, and obsolescence rate all play important roles in determining the impact of EPA's program on innovative activity. These factors are expected to be highly variable and product-specific.

7. *Impacts on small business*. EPA survey data suggest that 42 percent of companies potentially affected by the proposed rule may be small businesses. Though data were not available allowing the Agency to employ standard criteria for assessing the magnitude of small business impacts, the finding of a substantial portion of the regulated community to be small businesses prompted EPA to develop options to provide relief to such businesses. The options considered include reducing CBI substantiation requirements and the elimination of the $100 filing fee.

### *B. Request for Comment on Economic Issues*

Based on the analysis presented in the RIA, EPA's preliminary findings are that this proposed rule should not adversely affect either innovation or international competitiveness in biotechnology; to the contrary, EPA believes that this proposed rule will provide needed regulatory and procedural clarity under TSCA to enable the U.S. biotechnology industry to commercialize products while ensuring appropriate oversight to protect public health and the environment.

EPA nevertheless believes that this proposed rule should continue to be evaluated in light of its potential impact on innovation and international competitiveness. To this end, the Agency is requesting public comment regarding the economic impacts associated with this proposed rule. Data or other information are specifically requested in connection with the following: rate of capital acquisition and critical factors affecting R&D capitalization; rate and magnitude of R&D expenditures;

data regarding actual submissions under the current policy, e.g., project development costs, regulatory burdens, development schedules and revenues.

### VI. Rulemaking Record and Electronic Availability of Documents

A record has been established for this proposed rule under docket number ''OPPTS–00049C.'' A public version of this record which does not include any information claimed as CBI (see Unit VII. of this preamble), is available for inspection from noon to 4 p.m., Monday through Friday, excluding legal holidays. The public record is located in the TSCA Nonconfidential Information Center (NCIC) (also known as the TSCA Public Docket Office), Rm. NE–B607, 401 M St., SW., Washington, DC 20460.

As part of an interagency ''streamlining'' initiative, EPA is making this proposed rule and certain support documents available electronically. They may be accessed through the Internet at: gopher.epa.gov.

EPA is very interested in learning whether persons have obtained these documents electronically and what their experiences were in doing so. Persons who comment on this proposed rule are encouraged to provide feedback on this electronic availability with their comments.

To obtain further information or to provide feedback on the electronic availability of these documents, please contact Juanita Geer (Telephone: 202–260–1532; FAX: 202–260–1657; Internet: geer.juanita@epamail.epa.gov). Please be advised that Ms. Geer will accept only feedback on the electronic availability of these documents; all comments on the substance of the proposed rule must be submitted to the docket above.

### VII. Public Record

EPA has established a public record for this rulemaking (docket control number OPPTS–00049C). The record includes all information considered by EPA in developing this proposed rule. The record now includes the following items:

1. All prior **Federal Register** Notices, and supporting public dockets, relating to the regulation of microbial products of biotechnology under TSCA. These include:

a. The 1984 Proposed Policy Statement (49 FR 50856, December 31, 1984).

b. The 1986 Policy Statement (51 FR 23302, June 26, 1986).

c. ''Biotechnology; Request for Comment on Regulatory Approach'', 54 FR 7027, February 15, 1989).

2. Public comments submitted in response to each of the above Notices, including the comments received at the September 1989 Meeting which was held to discuss TSCA regulatory options for oversight of R&D.

3. ''Principles for Federal Oversight of Biotechnology: Planned Introduction Into the Environment of Organisms With Modified Hereditary Traits'', Office of Science and Technology Policy, 55 FR 31118, July 31, 1990.

4. Reports of all BSAC meetings pertaining to this proposed rule.

5. The Regulatory Impact Analysis for this proposed rule.

6. Support documents and reports.

7. Records of all communications between EPA personnel and persons outside EPA pertaining to the development of this proposed rule. (This does not include any inter- or intra-agency memoranda, unless specifically noted in the Index of this docket.)

8. The docket also includes published literature that is cited in this document.

EPA will accept additional materials for inclusion in the record at any time between the date of publication of this proposed rule and the designation of the complete record. EPA will identify the complete rulemaking record by the date of promulgation of the final rule.

Comments received on this proposed rule, along with a complete Index of the docket for this rulemaking, is available to the public for inspection from noon to 4 p.m., Monday through Friday, except legal holidays, in the TSCA Nonconfidential Information Center, Rm. NE–102, 401 M St., SW., Washington, DC 20460. Only nonconfidential versions of documents are included in the public record.

### VIII. References

The following books, articles, and reports were used in preparing this notice and were cited in this notice by the number indicated below:

(1) U.S. Congress, Office of Technology Assessment. 1988. ''New Developments in Biotechnology - Field-Testing Engineered Organisms: Genetic and Ecological Issues'', OTA–BA–350. U.S. Government Printing Office, Washington, DC.

(2) U.S. Congress, Subcommittee on Investigations and Oversight, House Science, Space and Technology Committee. 1986. ''Issues in the Federal Regulation of Biotechnology: from Research to Releases.'' Washington, DC.

(3) U.S. Environmental Protection Agency, Office of General Counsel, Pesticides and Toxic Substances Division. 1983. ''Status of recombinant DNA and new life forms under Toxic Substances Control Act (TSCA). Washington, DC.

(4) U.S. Congress, Office of Technology Assessment, ''New Developments in Biotechnology - U.S. Investment in Biotechnology Summary,'' Vol. 4, p. 13. OTA–BA–401, U.S. Government Printing Office, Washington, DC.

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(11) Gill, D.M. 1982. ''Bacterial toxins: a table of lethal amounts.'' Microbiological Reviews 46(1): 86–94.

(12) Gill, D.M. 1987. ''Bacterial Toxins: description.'' Laskin, A.I. Lechevalier, H.A., eds. Pages 3–18 in CRC Handbook of Microbiology, 2nd edition, Volume VIII, Toxins Enzymes. CRC Press, Boca Raton, FL.

(13) Sayre, P.G. and Miller, R.V. 1991. ''Bacterial mobile genetic elements: Importance in assessing the environmental fate of genetically engineered sequences.'' Plasmid 26:151–171.

(14) Kokjohn, T.A. 1989. ''Transduction: mechanism and potential for gene transfer in the environment.'' Pages 73–97 in Levy, S.B. and Miller, R.V., eds. Gene Transfer in the Environment. McGraw-Hill Publishing Co., New York.

(15) Stotzky, G. 1989. ''Gene transfer among bacteria in soil.'' Pages 165–222 in Levy, S.B. and Miller, R.V., eds. Gene Transfer in the Environment. McGraw-Hill Publishing Co., New York.

(16) Saye, D.J. Miller, R.V. 1989. ''The aquatic environment: consideration of horizontal gene transmission in a diversified habitat.'' Pages 223–259 in Levy, S.B. and Miller, R.V., eds. Gene Transfer in the Environment. McGraw-Hill Publishing Co., New York.

(17) Jeffrey, W., Paul, J., and Stewart, G. 1990. ''Natural transformation of a Marine Vibrio Species by Plasmid DNA.'' Microbial Ecology 19:259–268.

(18) Lewin, B., ed. 1987. Pages 55–56 in ''Genes, Third Edition.'' John Wiley Sons, New York.

(19) Maki, H., Horiucki, T., and Sekiguchi, M. 1983. ''Structure and expression of the DNAQ mutator and RNase H genes of *Escherichia coli*: Overlap of the promoter regions.'' Proceedings of the National Academy of Sciences 80:7137–7141.

(20) Ippen-Ihler, K. 1989. ''Bacterial Conjugation.'' Pages 33–72 in Levy, S.B. and Miller, R.V., eds. 1989. Gene Transfer in the Environment. McGraw-Hill Publishing Co., New York.

(21) U.S. Environmental Protection Agency, Office of Toxic Substances, Economics Technology Division, Chemical Engineering Branch. 1991. ''Analysis of environmental releases and occupational exposure in support of proposed TSCA 5(h)(4) exemption.'' Washington, DC.

(22) Battelle. 1988. Final Report on Biosafety in Large-Scale rDNA Processing Facilities. 6 volume set. U.S. EPA, Risk Reduction Engineering Laboratory, Cincinnati, OH.

(23) National Institutes of Health, U.S. Department of Health Human Services. 1984. ''Meeting of the Large-Scale Review Working Group of the Recombinant DNA Advisory Committee.'' Recombinant DNA Bulletin 7(2): 68–74.

(24) Atlas, R. and Bartha, R. 1987. Microbial Ecology. Benjamin/ Cummings Publishing Company, Inc., Menlo Park, CA.

(25) Francki, R.I.B., Fauquet, C.M., Knudson, D.L., Brown, F. (eds.) 1991. Archives of Virology/ Supplementum 2. Springer-Verlag, NY., NY.

## IX. Regulatory Assessment Requirements

### *A. Executive Order 12866*

Under Executive Order 12866 (58 FR 51735, October 4, 1993), the Agency must determine whether the regulatory action is ''significant'' and therefore subject to review by the Office of Management and Budget (OMB) and the requirements of the Executive Order. Under section 3(f), the order defines a ''significant regulatory action'' as an action that is likely to result in a rule: (1) Having an annual effect on the economy of $100 million or more, or adversely and materially affecting a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local or tribal governments or communities (also referred to as ''economically significant''); (2) creating serious inconsistency or otherwise interfering with an action taken or planned by another agency; (3) materially altering the budgetary impacts of entitlement, grants, user fees, or loan programs or the rights and obligations of recipients thereof; or (4) raising novel legal or policy issues arising out of legal mandates, the President's priorities, or the principles set forth in this Executive Order.

Pursuant to the terms of this Executive Order, EPA has determined that this proposed rule is ''significant'' because it raises novel policy issues arising out of legal mandates. As such, this action was submitted to OMB for review, and any comments or changes made in response to OMB suggestions or recommendations have been documented in the public record.

### *B. Regulatory Flexibility Act*

Under the Regulatory Flexibility Act (5 U.S.C. 605(b)), EPA has analyzed the economic impact of this proposed rule on small businesses. A summary of this analysis appears in Unit V. of this preamble. This

proposed rule does not exempt small businesses. Preliminary analysis of the impacts of this proposed rule on small businesses indicates that the compliance costs may have a significant impact. Despite the uncertainties and data gaps faced by EPA in developing this analysis, EPA believes that it is prudent public policy to assume that the requirements of the Regulatory Flexibility Act (Pub. L. 96–354) have been triggered. EPA believes that review of certain new microorganisms under TSCA is important to ensure that there are no unreasonable risks to health and the environment, and that the mechanisms outlined in this proposed rule will lessen impacts on small business as much as possible.

The Regulatory Impact Analysis section on small business impacts (Section VIII of the RIA, which is part of the public record for this rulemaking) serves as the Initial Regulatory Flexibility Analysis required by the Regulatory Flexibility Act. EPA intends to revise this analysis prior to promulgation of the final rule. EPA requests comments on the methodology employed in this analysis and the results of this analysis.

*C. Paperwork Reduction Act*

The Office of Management and Budget (OMB) has approved the current Premanufacture Notification and SNUR program under the provisions of the Paperwork Reduction Act, 44 U.S.C. 3501 et seq. and has assigned OMB control number 2070–0012. This proposed rule, when promulgated, would modify those information collection requirements; an information collection request addressing these modifications has been submitted to OMB under the provisions of the Paperwork Reduction Act, 44 U.S.C. 3501 et seq.

Public reporting burden for this collection of information is estimated to average 473 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information.

Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing burden, to Chief, Information Policy Branch, 2136, U.S. Environmental Protection Agency, 401 M St., SW., Washington, DC 20460, and to the Office of Information and Regulatory Affairs, Office of Management and Budget, Washington, DC 20503, marked ''Attention: Desk Officer for EPA.'' The final rule will respond to any OMB or public comments on the information collection requirements contained in this proposal.

**List of Subjects in 40 CFR Parts 700, 720, 721, 723, and 725**

Environmental protection, Administrative practice and procedure, Biotechnology, Chemicals, Hazardous substances, Imports, Labeling, Microorganisms, Occupational safety and health, Reporting and recordkeeping requirements

Dated: August 19, 1994.

**Carol M. Browner,**

*Administrator.*

Therefore, it is proposed that 40 CFR Chapter I be amended as follows:

## PART 700—[AMENDED]

1. In part 700:

a. The authority citation for part 700 would continue to read as follows:

**Authority**: 15 U.S.C. 2625.

b. In § 700.43, by revising the introductory text and the definition of ''Section 5 notice'' and adding two definitions to read as follows:

### § 700.43 Definitions.

Definitions in section 3 of the Act (15 U.S.C. 2602), as well as definitions contained in § § 704.3, 720.3, and 725.3 of this chapter, apply to this subpart unless otherwise specified in this section. In addition, the following definitions apply:

*Consolidated microbial commercial activity notice or consolidated MCAN* means any MCAN submitted to EPA that covers more than one microorganism (each being assigned a separate MCAN number by EPA) as a result of a prenotice agreement with EPA.

* * * * *

*Microbial commercial activity notice* or *MCAN* means any notice for microorganisms submitted to EPA pursuant to section 5(a)(1) of the Act in accordance with subpart D of part 725 of this chapter.

* * * * *

*Section 5 notice* means any PMN, consolidated PMN, intermediate PMN, significant new use notice, exemption notice, exemption application, any MCAN or consolidated MCAN submitted under section 5 of TSCA.

* * * * *

c. In § 700.45 by adding paragraphs (b)(2)(vi), (e)(4)(iv), (e)(5)(iv), (f)(4), and revising paragraphs (c) and (f)(3) to read as follows:

### § 700.45 Fee payments.

* * * * *

(b) * * *

(2) * * *

(vi) *MCAN and consolidated MCAN*. Persons shall remit a fee of $2,500 for each MCAN or consolidated MCAN submitted.

(c) *No fee required*. Persons are exempt from remitting any fee for submissions under § § 720.38, 723.50, and subparts E, F, and G of part 725 of this chapter.

* * * * *

(e) * * *

(4) * * *

(iv) Each person who remits the fee identified in paragraph (b)(1) of this section for a MCAN for a microorganism shall include the words, ''The company identified in this notice is a small business concern under 40 CFR 700.43 and has remitted a fee of $100 in accordance with 40 CFR 700.45(d),'' in the certification required in § 725.25(b) of this chapter.

(5) * * *

(iv) Each person who remits a fee identified in paragraph (b)(2) of this

section for a MCAN for a microorganism shall include the words, ''The company identified in this notice has remitted the fee specified in 40 CFR 700.45(b),'' in the certification required in § 725.25(b) of this chapter.

(f) * * *

(3) The notice is incomplete under either § 720.65(c) or 725.33, of this chapter.

(4) That as of the date of submission of the notice: the microorganism that is the subject of a MCAN is not a new microorganism; nor is the use involving the microorganism a significant new use.

d. By revising § 700.49 to read as follows:

**§ 700.49 Failure to remit fees.**

EPA will not consider a section 5 notice to be complete unless the appropriate certification under § 700.45(e) is included and until the appropriate remittance under § 700.45(b) has been sent to EPA as provided in § 700.45(e) and received by EPA. EPA will notify the submitter that the section 5 notice is incomplete in accordance with § § 720.65(c) and 725.33 of this chapter.

## PART 720 — [AMENDED]

2. In part 720:

a. The authority citation for part 720 would continue to read as follows:

**Authority**: 15 U.S.C. 2604, 2607, and 2613.

b. In § 720.1, by revising the first sentence and adding a sentence to read as follows:

**§ 720.1 Scope.**

This part establishes procedures for the reporting of new chemical substances by manufacturers and importers under section 5 of the Toxic Substances Control Act, 15 U.S.C. 2604. This part applies to microorganisms only to the extent provided by part 725 of this chapter.

* * *

## PART 721 — [AMENDED]

3. In part 721:

a. The authority citation for part 721 would continue to read as follows:

**Authority**: 15 U.S.C. 2604, 2607, and 2625(c).

b. In § 721.1(a), by revising the first sentence to read as follows:

**§ 721.1 Scope and applicability.**

This part identifies uses of chemical substances, except for microorganisms regulated under part 725 of this chapter, which EPA has determined are significant new uses under the authority of section 5(a)(2) of the Toxic Substances Control Act.

* * *

## PART 723 — [AMENDED]

4. In part 723:

a. The authority citation for part 723 would continue to read as follows:

**Authority**: 15 U.S.C. 2604.

b. In § 723.50, by revising paragraph (a)(1) to read as follows:

**§ 723.50 Chemical substances manufactured in quantities of 1,000 kilograms or less per year.**

(a) *Purpose and scope*. (1) This section grants an exemption from the premanufacture notice requirements of section 5(a)(1)(A) of the Toxic Substances Control Act (15 U.S.C. 2604(a)(1)(A)) for the manufacture of certain chemical substances manufactured in quantities of 1,000 kilograms or less per year. This section does not apply to microorganisms regulated under part 725 of this chapter.

* * * * *

c. In § 723.175, by revising paragraph (a)(1) to read as follows:

**§ 723.175 Chemical substances used in or for the manufacture or processing of instant photographic and peel-apart film articles.**

(a) *Purpose and scope*. (1) This section grants an exemption from the premanufacture notice requirements of section 5(a)(1)(A) of the Toxic Substances Control Act (15 U.S.C. 2604(a)(1)(A)) for the manufacture and processing of new chemical substances used in or for the manufacture or processing of instant photographic and peel-apart film articles. This section does not apply to microorganisms regulated under part 725 of this chapter.

* * * * *

d. In § 723.250, by revising paragraph (a)(1) to read as follows:

**§ 723.250 Polymers.**

(a) *Purpose and scope*. (1) This section grants an exemption from the premanufacture notice requirements of section 5(a)(1)(A) of the Toxic Substances Control Act (15 U.S.C. 2604(a)(1)(A)) for the manufacture of certain polymers. This section does not apply to microorganisms regulated under part 725 of this chapter.

* * * * *

5. Part 725 is added to read as follows:

## PART 725—REPORTING REQUIREMENTS AND REVIEW PROCESSES FOR MICROORGANISMS

### Subpart A—General Provisions and Applicability

Sec.

725.1 Scope and purpose.
725.3 Definitions.
725.8 Coverage of this part.
725.12 Identification of microorganisms for Inventory and other listing purposes.
725.15 Determining applicability when microorganism identity or use is confidential or uncertain.
725.17 Consultation with EPA.

### Subpart B—Administrative Procedures

725.20 Scope and purpose.
725.25 General administrative requirements.
725.27 Submissions.
725.28 Notice that submission is not required.
725.29 EPA acknowledgement of receipt of submission.
725.32 Errors in the submission.
725.33 Incomplete submissions.
725.36 New information.
725.40 Notice in the **Federal Register**.
725.50 EPA review.
725.54 Suspension of the review period.

725.56 Extension of the review period.
725.60 Withdrawal of submission by the submitter.
725.65 Recordkeeping.
725.67 Applications to exempt new microorganisms from this part.
725.70 Compliance.
725.75 Inspections.

**Subpart C—Confidentiality and Public Access to Information**

725.80 General provisions for confidentiality claims.
725.85 Microorganism identity.
725.88 Uses of a microorganism.
725.92 Data from health and safety studies of microorganisms.
725.94 Substantiation requirements.
725.95 Public file.

**Subpart D—Microbial Commercial Activities Notification Requirements**

725.100 Scope and purpose.
725.105 Persons who must report.
725.110 Persons not subject to this subpart.
725.150 Procedural requirements for this subpart.
725.155 Information to be included in the MCAN.
725.160 Submission of health and environmental effects data.
725.170 EPA review of the MCAN.
725.190 Notice of commencement of manufacture or import.

**Subpart E—Exemptions for Research and Development Activities**

725.200 Scope and purpose.
725.205 Persons who may report under this subpart.
725.232 Activities subject to the jurisdiction of other Federal programs or agencies.
725.234 Activities conducted inside a structure.
725.235 Conditions of exemption for activities conducted inside a structure.
725.238 Activities conducted outside a structure.
725.239 Use of specific microorganisms in activities conducted outside a structure.
725.250 Procedural requirements for this subpart.
725.255 Information to be included in the TERA.
725.260 Submission of health and environmental effects data.
725.270 EPA review of the TERA.
725.288 Revocation or modification of TERA approval.

**Subpart F—Exemptions for Test Marketing**

725.300 Scope and purpose.
725.305 Persons who may report under this subpart.
725.350 Procedural requirements for this subpart.
725.355 Information to be included in the TME application.
725.370 EPA review of the TME application.

**Subpart G—Exemption for Microorganisms in General Commercial Use**

725.400 Scope and purpose.
725.420 Recipient microorganisms.
725.421 Introduced genetic material.
725.422 Physical containment and control technologies.
725.424 Requirements for the Tier I exemption.
725.426 Liability of the manufacturer or importer who uses the Tier I exemption.
725.428 Requirements for the Tier II exemption.
725.450 Procedural requirements for the Tier II exemption.
725.455 Information to be included in the Tier II exemption request.
725.470 EPA review of the Tier II exemption request.

**Subparts H—K [Reserved]**

**Subpart L—Additional Procedures Applicable to Reporting on Significant New Uses of Microorganisms**

725.900 Scope and purpose.
725.910 Persons excluded from reporting of significant new uses.
725.912 Exemptions.
725.920 Exports and imports.
725.950 Additional recordkeeping requirements for reporting of significant new uses.
725.975 EPA approval of alternative control measures.
725.980 Expedited procedures for issuing significant new use rules for microorganisms subject to section 5(e) orders.
725.984 Modification or revocation of certain notification requirements.

**Subpart M—Significant New Uses for Specific Microorganisms—[Reserved]**

**Authority**: 15 U.S.C. 2604, 2607, 2613, and 2625.

**Subpart A—General Provisions and Applicability**

**§ 725.1 Scope and purpose.**

(a) This part establishes reporting requirements under section 5 of TSCA for manufacturers, importers, and processors of microorganisms for commercial purposes.

(b) TSCA section 5 covers chemical substances as defined under TSCA section 3. Because EPA interprets the section 3 definition to include microorganisms, section 5 also covers microorganisms. Unless otherwise specifically stated in the Code of Federal Regulations, TSCA section 5 authority over microorganisms (as distinguished from other chemical substances) will be implemented under this part.

(c) Microorganisms subject to reporting as new microorganisms will be those which are intergeneric. In addition, any microorganism subject to TSCA jurisdiction may be subject to reporting, if EPA determines by rule that the microorganism is being manufactured, imported, or processed for a significant new use.

(d) This subpart A describes the general organization for this part and contains definitions generally applicable to this part.

(e) Subpart B of this part describes general administrative procedures applicable to microorganisms subject to this part.

(f) Subpart C of this part establishes requirements for handling confidential business information (CBI) and public access to information submitted under this part.

(g) Subpart D of this part describes the persons and microorganisms subject to Microorganism Commercial Activity Notices (MCANs), prescribes the content of MCANs, and establishes procedures for reviewing MCANs.

(h) Subpart E of this part establishes reporting requirements and EPA review procedures for the TSCA Experimental Release Application (TERA) for microorganisms intentionally tested in the environment during commercial research and

development activities. Subpart E of this part also identifies microorganisms and classes of microorganisms exempt from research and development reporting.

(i) Subpart F of this part establishes procedures for obtaining test marketing exemptions (TMEs) for microorganisms.

(j) Subpart G of this part identifies microorganisms in general commercial use under certain conditions of containment that are eligible for Tier I and Tier II exemptions from subpart D reporting. Subpart G of this part establishes reporting requirements and procedures for expedited review of the Tier II exemption request.

(k) Subpart L of this part describes additional requirements applicable to reporting on microorganisms subject to significant new use rules under TSCA section 5(a)(2). All significant new uses of microorganisms are subject to the MCAN requirements in subpart D of this part.

(l) Subpart M of this part identifies specific significant new uses of microorganisms subject to subpart D reporting.

### § 725.3 Definitions.

Definitions in section 3 of the Act (15 U.S.C. 2602), as well as definitions contained in § § 704.3, 720.3, and 721.3 of this chapter, apply to this part unless otherwise specified in this section. In addition, the following definitions apply to this part:

*Consolidated microbial commercial activity notice* or *consolidated MCAN* means any MCAN submitted to EPA that covers more than one microorganism (each being assigned a separate MCAN number by EPA) as a result of a prenotice agreement with EPA.

*Containment and/or inactivation controls* means any combination of engineering, mechanical, procedural, or biological controls designed and operated to restrict environmental release of viable microorganisms from a structure.

*Director* means the Director of the EPA Office of Pollution Prevention and Toxics.

*Exemption request* means any application submitted to EPA under subparts E, F, or G of this part.

*General commercial use* means use for commercial purposes other than research and development.

*Genome* means the sum total of chromosomal and extrachromosomal genetic material of an isolate and any descendants derived under pure culture conditions from that isolate.

*Health and safety study of a microorganism* or *health and safety study* means any study of any effect of a microorganism or microbial mixture on health or the environment or on both, including underlying data and epidemiological studies, studies of occupational exposure to a microorganism or microbial mixture, toxicological, clinical, and ecological, or other studies of a microorganism or microbial mixture, and any test performed under the Act. Microorganism identity is always part of a health and safety study of a microorganism.

(1) It is intended that the term ''health and safety study of a microorganism'' be interpreted broadly. Not only is information which arises as a result of a formal, disciplined study included, but other information relating to the effects of a microorganism or microbial mixture on health or the environment is also included. Any data that bear on the effects of a microorganism on health or the environment would be included.

(2) Examples include:

(i) Tests for ecological or other environmental effects on invertebrates, fish, or other animals, and plants, including: Acute toxicity tests, chronic toxicity tests, critical life stage tests, behavioral tests, algal growth tests, seed germination tests, plant growth or damage tests, microbial function tests, bioconcentration or bioaccumulation tests, and model ecosystem (microcosm) studies.

(ii) Long- and short-term tests of mutagenicity, carcinogenicity, or teratogenicity; dermatoxicity; cumulative, additive, and synergistic effects; and acute, subchronic, and chronic effects.

(iii) Assessments of human and environmental exposure, including workplace exposure, and impacts of a particular microorganism or microbial mixture on the environment, including surveys, tests, and studies of: Survival and transport in air, water, and soil; ability to exchange genetic material with other microorganisms, ability to colonize human or animal guts, and ability to colonize plants.

(iv) Monitoring data, when they have been aggregated and analyzed to measure the exposure of humans or the environment to a microorganism.

(v) Any assessments of risk to health and the environment resulting from the manufacture, processing, distribution in commerce, use, or disposal of the microorganism.

*Inactivation* means that living microorganisms are rendered nonviable. ''Introduced genetic material'' means genetic material that is added to, and remains as a component of, the genome of the recipient.

*Intergeneric microorganism* means a microorganism that is formed by the deliberate combination of genetic material from organisms of different taxonomic genera, including mobile genetic elements. The term ''intergeneric microorganism'' does not include a microorganism which contains genetic material consisting of only well-characterized, non-coding regulatory regions from another genus.

*Introduced genetic material* means genetic material that is added to, and remains as a component of, the genome of the recipient.

*Manufacture, import, or process for commercial purposes* means: (1) To import, produce, manufacture, or process with the purpose of obtaining an immediate or eventual commercial advantage for the manufacturer, importer, or processor, and includes, among other things, ''manufacture'' or ''processing'' of any amount of a microorganism or microbial mixture:

(i) For commercial distribution, including for test marketing.

(ii) For use by the manufacturer, including use for product research and development or as an intermediate.

(2) The term also applies to substances that are produced coincidentally during the manufacture, processing, use, or disposal of another microorganism or microbial mixture, including byproducts that are separated from that other microorganism or microbial mixture and impurities that remain in that microorganism or microbial mixture. Byproducts and impurities without separate commercial value are nonetheless produced for the purpose of obtaining a commercial advantage, since they are part of the manufacture or processing of a microorganism for commercial purposes.

*Microbial commercial activity notice* or *MCAN* means a notice for microorganisms submitted to EPA pursuant to subpart D of this part.

*Microbial mixture* means any combination of microorganisms or microorganisms and other chemical substances, if the combination does not occur in nature and is not an article.

*Microorganism* means an organism classified in the kingdoms Monera (or Procaryotae), Protista, Fungi, and the Chlorophyta and the Rhodophyta of the Plantae, and a virus or virus-like particle.

*Mobile genetic element* or *MGE* means an element of genetic material that has the ability to move genetic material within and between organisms. ''Mobile genetic elements'' include all plasmids, viruses, transposons, insertion sequences, and other classes of elements with these general properties.

*New microorganism* means a microorganism not included on the TSCA Inventory.

*Small quantities solely for research and development* (or ''small quantities solely for purposes of scientific experimentation or analysis or research on, or analysis of, such substance or another substance, including such research or analysis for development of a product'') means quantities of a microorganism manufactured, imported, or processed or proposed to be manufactured, imported, or processed solely for research and development that meet the requirements of § 725.234.

*Structure* means a building or vessel which effectively surrounds and encloses the microorganism and includes features designed to restrict the microorganism from leaving.

*Submission* means any MCAN or exemption request submitted to EPA under this part.

*Technically qualified individual* means a person or persons (1) Who, because of education, training, or experience, or a combination of these factors, is capable of understanding the health and environmental risks associated with the microorganism which is used under his or her supervision, (2) who is responsible for enforcing appropriate methods of conducting scientific experimentation, analysis, or microbiological research to minimize such risks, and (3) who is responsible for the safety assessments and clearances related to the procurement, storage, use, and disposal of the microorganism as may be appropriate or required within the scope of conducting a research and development activity.

*TSCA Experimental Release Application* or *TERA* means an exemption request for a research and development activity, which is not eligible for a full exemption from reporting under § 725.232, 725.234, or 725.238 of this part, submitted to EPA in accordance with subpart E of this part.

*Well-characterized, non-coding regulatory region* means a segment of genetic material for which:

(1) The exact nucleotide base sequences of the regulatory region and any inserted flanking nucleotides are known and documented.

(2) The regulatory region and any inserted flanking nucleotides do not code for protein, peptide, or functional ribonucleic acid molecules.

(3) The regulatory region solely controls the activity of other regions that code for protein or peptide molecules or act as recognition sites for the initiation of nucleic acid or protein synthesis.

### § 725.8 Coverage of this part.

(a) *Microorganisms subject to this part.* Only microorganisms which are manufactured, imported, or processed for commercial purposes, as defined in § 725.3 of this part, are subject to the requirements of this part.

(b) *Microoganisms automatically included on the Inventory.* Microorganisms that are not intergeneric are automatically included on the TSCA Inventory.

(c) *Microorganisms not subject to this part.* The following microorganisms are not subject to this part, either because they are not subject to TSCA jurisdiction or are not subject to reporting under TSCA section 5.

(1) Any microorganism which would be excluded from the definition of ''chemical substance'' in section 3 of TSCA and § 720.3(e) of this chapter.

(2) Any microbial mixture as defined in § 725.3 of this part. This exclusion applies only to a microbial mixture as a whole and not to any microorganisms and other chemical substances which are part of the microbial mixture.

(3) Any microorganism that is manufactured and processed solely for export if the following conditions are met:

(i) The microorganism is labeled in accordance with section 12(a)(1)(B) of TSCA, when the microorganism is distributed in commerce.

(ii) The manufacturer and processor can document at the commencement of manufacturing or processing that the person to whom the microorganism will be distributed intends to export it or process it solely for export as defined in § 721.3 of this chapter.

### § 725.12 Identification of microorganisms for Inventory and other listing purposes.

To identify and list microorganisms on the Inventory, both taxonomic designations and

supplemental information will be used. The supplemental information required in paragraph (b) of this section will be used to specifically describe an individual microorganism on the Inventory. Submitters must provide the supplemental information required by paragraph (b) of this section to the extent necessary to enable a microorganism to be accurately and unambiguously identified on the Inventory.

(a) *Taxonomic designation*. The taxonomic designation of a microorganism must be provided for the donor organism and the recipient microorganism to the level of strain, as appropriate. These designations must be substantiated by a letter from a culture collection, literature references, or the results of tests conducted for the purpose of taxonomic classification. Upon EPA's request to the submitter, data supporting the taxonomic designation must be provided to EPA. The genetic history of the recipient microorganism should be documented back to the isolate from which it was derived.

(b) *Supplemental information*. The supplemental information described in paragraphs (b)(1) and (b)(2) of this section is required to the extent that it enables a microorganism to be accurately and unambiguously identified.

(1) *Phenotypic information*. Phenotypic information means pertinent traits that result from the interaction of a microorganism's genotype and the environment in which it is intended to be used and may include intentionally added biochemical and physiological traits.

(2) *Genotypic information*. Genotypic information means the pertinent and distinguishing genotypic characteristics of a microorganism, such as the identity of the introduced genetic material and the methods used to construct the reported microorganism. This also may include information on the vector construct, the cellular location, and the number of copies of the introduced genetic material.

**§ 725.15 Determining applicability when microorganism identity or use is confidential or uncertain.**

(a) *Consulting EPA*. Persons intending to conduct activities involving microorganisms may determine their obligations under this part by consulting the TSCA Inventory or the microorganisms and uses specified in § 725.239 or subpart M of this part. This section establishes procedures for EPA to assist persons in determining whether the microorganism or the use is listed on the Inventory or in § 725.239 or subpart M of this part.

(1) Confidential identity or use. In some cases it may not be possible to directly determine if a specific microorganism is listed, because portions of that entry may contain generic information to protect confidential business information (CBI). If any portion of the microorganism's identity or use has been claimed CBI, that portion does not appear on the public version of the Inventory, in § 725.239 or in subpart M of this part. Instead, it is contained in a confidential version held in EPA's Confidential Business Information Center (CBIC). The public versions contain generic information which masks the confidential business information. A person who intends to conduct an activity involving a microorganism or use whose entry is described with generic information will need to inquire of EPA whether the unreported microorganism or use is on the confidential version.

(2) Uncertain microorganism identity. The current state of scientific knowledge leads to some imprecision in describing a microorganism. As the state of knowledge increases, EPA will be developing policies to determine whether one microorganism is equivalent to another. Persons intending to conduct activities involving microorganisms may inquire of EPA whether the microorganisms they intend to manufacture, import, or process are equivalent to specific microorganisms described on the Inventory, in § 725.239 or subpart M of this part.

(b) *Requirement of bona fide intent*. (1) EPA will answer the inquiries described in paragraph (a) of this section only if the Agency determines that the person has a *bona fide* intent to conduct the activity for which reporting is required or for which any exemption may apply.

(2) To establish a *bona fide* intent to manufacture, import, or process a microorganism, the person who intends to manufacture, import, or process the microorganism must submit the following information in writing to the Office of Pollution Prevention and Toxics, Document Control Officer, 7407, 401 M St., SW., Washington, DC 20460, ATTN: BIOTECH *bona fide* submission.

(i) Taxonomic designations and supplemental information required by § 725.12.

(ii) A signed statement certifying that the submitter intends to manufacture, import, or process a microorganism for commercial purposes.

(iii) A description of research and development activities conducted with the microorganism to date, demonstration of the submitter's ability to produce or obtain the microorganism from a foreign manufacturer, and the purpose for which the person will manufacture, import, or process the microorganism.

(iv) An indication of whether a related microorganism was previously reviewed by the Agency to the extent known by the submitter.

(c) If an importer or processor cannot provide all the information required by paragraph (b) of this section, because it is claimed as confidential business information by its foreign manufacturer or supplier, the foreign manufacturer or supplier may supply the information directly to EPA.

(d) EPA will review the information submitted by the manufacturer, importer, or processor under this paragraph to determine whether that person has shown a *bona fide* intent to manufacture,

import, or process the microorganism. If necessary, EPA will compare this information to the information requested for the confidential microorganism under § 725.85(b)(3)(iii).

(e) In order for EPA to make a conclusive determination of the microorganism's status, the proposed manufacturer, importer, or processor must show a *bona fide* intent to manufacture, import, or process the microorganism and must provide sufficient information to establish identity unambiguously. After sufficient information has been provided, EPA will inform the manufacturer, importer, or processor whether the microorganism is subject to this part and if so, which sections of this part apply.

(f) If the microorganism is found on the confidential version of the Inventory, in § 725.239 or subpart M of this part, EPA will notify the person(s) who originally reported the microorganism that another person (whose identity will remain confidential, if so requested) has demonstrated a *bona fide* intent to manufacture, import, or process the microorganism and therefore was told that the microorganism is subject to this part.

(g) A disclosure to a person with a bona fide intent to manufacture, import, or process a particular microorganism that the microorganism is subject to this part will not be considered a public disclosure of confidential business information under section 14 of the Act.

(h) EPA will answer an inquiry on whether a particular microorganism is subject to this part within 30 days after receipt of a complete submission under paragraph (b) of this section.

### § 725.17 Consultation with EPA.

Persons may consult with EPA, either in writing or by telephone, about their obligations under this part. Written consultation is preferred. Written inquiries should be sent to the following address: Environmental Assistance Division (7408), Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency, 401 M St., SW., Washington, DC 20460, ATTN: Biotechnology Notice Consultation. Persons wishing to consult with EPA by telephone should call (202) 554–1404; hearing impaired TDD (202) 554–0551.

## Subpart B—Administrative Procedures

### § 725.20 Scope and purpose.

This subpart describes general administrative procedures applicable to all persons who submit MCANs and exemption requests to EPA under section 5 of the Act for microorganisms.

### § 725.25 General administrative requirements.

(a) *General*. (1) Each person who is subject to the notification provisions of this part must complete, sign, and submit a MCAN or exemption request containing the information as required for the appropriate submission under this part. Except as otherwise provided, each submission must include all referenced attachments. All information in the submission (unless certain attachments appear in the open scientific literature) must be in English. All information submitted must be true and correct.

(2) In addition to specific information required, the submitter should submit all information known to or reasonably ascertainable by the submitter that would permit EPA to make a reasoned evaluation of the human health and environmental effects of the microorganism and any microbial mixture or article that may contain the microorganism.

(b) *Certification*. Persons submitting MCANs and exemption requests to EPA under this part, and material related to their reporting obligations under this part, must attach the following statement to any information submitted to EPA:

I certify that to the best of my knowledge and belief: The company named in this submission intends to manufacture, import, or process for a commercial purpose, other than in small quantities solely for research and development, the microorganism identified in this submission. All information provided in this submission is complete and truthful as of the date of submission. I am including with this submission all test data in my possession or control and a description of all other data known to or reasonably ascertainable by me as required by 40 CFR 725.160 or 725.260.

This statement must be signed and dated by an authorized official of the submitter.

(c) *Where to submit information under this part.* Persons submitting MCANs and exemption requests to EPA under this part, and material related to their reporting obligations under this part, must send them to: TSCA Document Processing Center (7407), Rm. L–100, Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency, 401 M St., SW., Washington, DC 20460.

(d) *General requirements for submission of data*. (1) Submissions under this part must include the information described in § 725.155, 725.255, 725.355, or 725.455, as appropriate, to the extent such information is known to or reasonably ascertainable by the submitter.

(2) In accordance with § 725.160 or 725.260, as appropriate, the submission must also include any test data in the submitter's possession or control and descriptions of other data which are known to or reasonably ascertainable by the submitter and which concern the health and environmental effects of the microorganism.

(e) *Agency or joint submissions*. (1) A manufacturer or importer may designate an agent to submit the MCAN or exemption request. Both the manufacturer or importer and the agent must sign the certification required in paragraph (b) of this section.

(2) A manufacturer or importer may authorize another person (e.g., a foreign manufacturer or supplier, or a toll manufacturer) to report some of the information required in

theMCAN or exemption request to EPA on its behalf. If separate portions of a joint submission are not submitted together, the submitter must indicate which information will be supplied by another person and identify that person. The manufacturer or importer and any other person supplying the information must sign the certification required by paragraph (b) of this section.

(3) If EPA receives a submission which does not include the information required, which the submitter indicates that it has authorized another person to provide, the review period will not begin until EPA receives all of the required information.

(f) *Microorganisms subject to a section 4 test rule*. (1) Except as provided in paragraph (f)(3) of this section, if (i) A person intends to manufacture or import a new microorganism which is subject to the notification requirements of this part, and (ii) the microorganism is subject to a test rule promulgated under section 4 of the Act before the notice is submitted, section 5(b)(1) of the Act requires the person to submit the test data required by the testing rule with the notice. The person must submit the data in the form and manner specified in the test rule and in accordance with § 725.160. If the person does not submit the test data, the submission is incomplete and EPA will follow the procedures in § 725.33.

(2) If EPA has granted the submitter an exemption under section 4(c) of the Act from the requirement to conduct tests and submit data, the person may not file a MCAN or TERA until EPA receives the test data.

(3) If EPA has granted the submitter an exemption under section 4(c) of the Act and if another person previously has submitted the test data to EPA, the exempted person may either submit the test data or provide the following information as part of the notice:

(i) The name, title, and address of the person who submitted the test data to EPA.

(ii) The date the test data were submitted to EPA.

(iii) A citation for the test rule.

(iv) A description of the exemption and a reference identifying it.

(g) *Microorganisms subject to a section 5(b)(4) rule*. (1) If a person (i) Intends to manufacture or import a microorganism which is subject to the notification requirements of this part and which is subject to a rule issued under section 5(b)(4) of the Act; and (ii) is not required by a rule issued under section 4 of the Act to submit test data for the microorganism before the filing of a submission, the person must submit to EPA data described in paragraph (g)(2) of this section at the time the submission is filed.

(2) Data submitted under paragraph (g)(1) of this section must be data which the person submitting the notice believes show that the manufacture, processing, distribution in commerce, use, and disposal of the microorganism, or any combination of such activities, will not present an unreasonable risk of injury to health or the environment.

(h) *Data that need not be submitted*. Specific data requirements are listed in subparts D, E, F, G, and L of this part. The following is a list of data that need not be submitted under this part:

(1) Data previously submitted to EPA. (i) A person need not submit any data previously submitted to EPA with no claims of confidentiality if the new submission includes: the office or person to whom the data were submitted; the date of submission; and, if appropriate, a standard literature citation as specified in § 725.160(a)(3)(ii).

(ii) For data previously submitted to EPA with a claim of confidentiality, the person must resubmit the data with the new submission and any claim of confidentiality, under § 725.80.

(2) Efficacy data. This part does not require submission of any data related solely to product efficacy. However, including efficacy data will improve EPA's ability to assess the benefits of the use of the microorganism. This does not exempt a person from submitting any of the data specified in § 725.160 or 725.260.

(3) Non-U.S. exposure data. This part does not require submission of any data which relates only to exposure of humans or the environment outside the United States. This does not exclude nonexposure data such as data on health effects (including epidemiological studies), ecological effects, physical and chemical properties, or environmental fate characteristics.

### § 725.27 Submissions.

Each person who is required to submit information under this part must submit the information in the form and manner set forth in the appropriate subpart.

(a) Requirements specific to MCANs are described in § § 725.150 through 725.160.

(b) Requirements specific to TERAs are described in § § 725.250 through 725.260.

(c) Requirements specific to test marketing exemptions (TMEs) are described in § § 725.350 and 725.355.

(d) Requirements specific to Tier I and Tier II exemptions for certain general commercial uses are described in § § 725.424 through 725.460.

(e) Additional requirements specific to significant new uses for microorganisms are described at § 725.950.

### § 725.28 Notice that submission is not required.

When EPA receives a MCAN or exemption request, EPA will review it to determine whether the microorganism is subject to the requirements of this part. If EPA determines that the microorganism is not subject to these requirements, EPA will notify the submitter that section 5 of the Act does not prevent the manufacture, import, or processing of the microorganism and that the submission is not needed.

**§ 725.29 EPA acknowledgement of receipt of submission.**

(a) EPA will acknowledge receipt of each submission by sending the submitter a letter that identifies the number assigned to the new microorganism and the date on which the review period begins. The review period will begin on the date the MCAN or exemption request is received by the Office of Pollution Prevention and Toxics Document Control Officer.

(b) The acknowledgement does not constitute a finding by EPA that the submission is in compliance with this part.

**§ 725.32 Errors in the submission.**

(a) Within 30 days of receipt of the submission, EPA may request that the submitter remedy errors in the submission. The following are examples of such errors:

(1) Failure to date the submission.

(2) Typographical errors that cause data to be misleading or answers to any questions to be unclear.

(3) Contradictory information.

(4) Ambiguous statements or information.

(b) In the request to correct the submission, EPA will explain the action which the submitter must take to correct the submission.

(c) If the submitter fails to correct the submission within 15 days of receipt of the request, EPA may extend the review period.

**§ 725.33 Incomplete submissions.**

(a) A submission under this part is not complete, and the review period does not begin, if:

(1) The wrong person files the submission.

(2) The submitter does not attach and sign the certification statement as required by § 725.25(b).

(3) Some or all of the information in the submission or any attachments are not in English, except for published scientific literature.

(4) The submitter does not provide information that is required by sections 5(d)(1)(B) and (C) of the Act and § 725.160 or 725.260, as appropriate.

(5) The submitter does not provide information required by § 725.25, 725.155, 725.255, 725.355, or 725.455, as appropriate, or indicate that it is not known to or reasonably ascertainable by the submitter.

(6) The submitter has asserted confidentiality claims and has failed to:

(i) Submit a second copy of the submission with all confidential information deleted for the public file, as required by § 725.80(b)(2).

(ii) Comply with the substantiation requirements as described in § 725.94.

(7) The submitter does not include any information required by section 5(b)(1) of the Act and pursuant to a rule promulgated under section 4 of the Act, as required by § 725.25(f).

(8) The submitter does not submit data which the submitter believes show that the microorganism will not present an unreasonable risk of injury to health or the environment, if EPA has listed the microorganism under section 5(b)(4) of the Act, as required in § 725.25(g).

(9) For MCANs, the submitter does not remit the fees required by § 700.45(b)(1) or (b)(2)(vi) of this chapter.

(b)(1) If EPA receives an incomplete submission under this part, the Director, or a designee, will notify the submitter within 30 days of receipt that the submission is incomplete and that the review period will not begin until EPA receives a complete submission.

(2) If EPA obtains additional information during the review period for any submission that indicates the original submission was incomplete, the Director, or a designee, may declare the submission incomplete within 30 days after EPA obtains the additional information and so notify the submitter.

(c) The notification that a submission is incomplete under paragraph (b) of this section will include:

(1) A statement of the basis of EPA's determination that the submission is incomplete.

(2) The requirements for correcting the incomplete submission.

(3) Information on procedures under paragraph (d) of this section for filing objections to the determination or requesting modification of the requirements for completing the submission.

(d) Within 10 days after receipt of notification by EPA that a submission is incomplete, the submitter may file written objections requesting that EPA accept the submission as complete or modify the requirements necessary to complete the submission.

(e)(1) EPA will consider the objections filed by the submitter. The Director, or a designee, will determine whether the submission was complete or incomplete, or whether to modify the requirements for completing the submission. EPA will notify the submitter in writing of EPA's response within 10 days of receiving the objections.

(2) If the Director, or a designee, determines, in response to the objection, that the submission was complete, the review period will be deemed suspended on the date EPA declared the submission incomplete, and will resume on the date that the submission is declared complete. The submitter need not correct the submission as EPA originally requested. If EPA can complete its review within the review period beginning on the date of the submission, the Director, or a designee, may inform the submitter that the running of the review period will resume on the date EPA originally declared it incomplete.

(3) If the Director, or a designee, modifies the requirements for completing the submission or concurs with EPA's original determination, the review period will begin when EPA receives a complete submission.

(f) Materially false or misleading statements. If EPA discovers at any time that a person submitted materially false or misleading statements in information submitted under this part, EPA may find that the submission was incomplete from the date it was submitted, and take any other appropriate action.

**§ 725.36 New information.**

(a) During the review period, if a submitter possesses, controls, or knows of new information that materially adds to, changes, or otherwise makes significantly more complete the information included in the MCAN or exemption request, the submitter must send that information to the address listed in § 725.25(c) within 10 days of receiving the new information, but no later than 5 days before the end of the review period.

(b) The new submission must clearly identify the submitter, the MCAN or exemption request to which the new information is related, and the number assigned to that submission by EPA, if known to the submitter.

(c) If the new information becomes available during the last 5 days of the review period, the submitter must immediately inform the EPA contact for that submission by telephone of the new information.

**§ 725.40 Notice in the Federal Register.**

(a) *Filing of Federal Register notice*. After EPA receives a MCAN or an exemption request under this part, EPA will issue a notice in the **Federal Register** including the information specified in paragraph (b) of this section.

(b) *Contents of notice*. (1) In the public interest, the specific microorganism identity listed in the submission will be published in the **Federal Register** unless the submitter has claimed the microorganism identity confidential. If the submitter claims confidentiality, a generic name will be published in accordance with § 725.85.

(2) The categories of use of the microorganism will be published as reported in the submission unless this information is claimed confidential. If confidentiality is claimed, the generic information which is submitted under § 725.88 will be published.

(3) A list of information submitted in accordance with § 725.160(a), 725.255, 725.260, 725.355, or 725.455, as appropriate, will be published.

(4) The submitter's identity will be published, unless the submitter has claimed it confidential.

(c) *Publication of exemption decisions*. Following the expiration of the appropriate review period for the exemption request, EPA will issue a notice in the **Federal Register** indicating whether the request has been approved or denied and the reasons for the decision.

**§ 725.50 EPA review.**

(a) *MCANs*. The review period specified in section 5(a) of the Act for MCANs runs for 90 days from the date the Document Control Officer receives a complete submission, or the date EPA determines the submission is complete under § 725.33, unless the Agency extends the review period under section 5(c) of TSCA and § 725.56.

(b) *Exemption requests*. The review period starts on the date the Document Control Officer receives a complete exemption request, or the date EPA determines the request is complete under § 725.33, unless the Agency extends the review period under § 725.56. The review periods for exemption requests run as follows:

(1) *TERAs*. The review period for TERAs is 60 days.

(2) *TMEs*. The review period for TMEs is 45 days.

(3) *Tier II exemption requests*. The review period for Tier II exemption requests is 45 days.

**§ 725.54 Suspension of the review period.**

(a) A submitter may voluntarily suspend the running of the review period if the Director, or a designee, agrees. If the Director does not agree, the review period will continue to run, and EPA will notify the submitter. A submitter may request a suspension at any time during the review period. The suspension must be for a specified period of time.

(b) A request for suspension may be made in writing to the address listed in § 725.25(c). The suspension also may be made orally, including by telephone, to the submitter's EPA contact for that submission. EPA will send the submitter a written confirmation that the suspension has been granted.

(1) An oral request may be granted for no longer than 15 days. To obtain a longer suspension, the Document Control Officer for the Office of Pollution Prevention and Toxics must receive written confirmation of the oral request. The review period is suspended as of the date of the oral request.

(2) If the submitter has not made a previous oral request, the running of the review period is suspended as of the date of receipt of the written request by the Document Control Officer for the Office of Pollution Prevention and Toxics.

**§ 725.56 Extension of the review period.**

(a) At any time during the review period, EPA may unilaterally determine that good cause exists to extend the review period specified for MCANs, or the exemption requests.

(b) If EPA makes such a determination, EPA:

(1) Will notify the submitter that EPA is extending the review period for a specified length of time and state the reasons for the extension.

(2) For MCANS, may issue a notice for publication in the **Federal Register** which states that EPA is extending the review period and gives the reasons for the extension.

(c) The total period of the extension may be for a period of up to the same length of time as specified for each type of submission in § 725.50. If the initial extension is for less than the total time allowed, EPA may make additional extensions. However, the sum of the extensions may not exceed the total allowed.

(d) The following are examples of situations in which EPA may find that good cause exists for extending the review period:

(1) EPA has reviewed the submission and is seeking additional information.

(2) EPA has received significant additional information during the review period.

(3) The submitter has failed to correct a submission after receiving EPA's request under § 725.32.

(4) EPA has reviewed the submission and determined that there is a significant possibility that the microorganism will be regulated under section 5(e) or section 5(f) of the Act, but EPA is unable to initiate regulatory action within the initial review period.

**§ 725.60 Withdrawal of submission by the submitter.**

(a) A submitter may withdraw a submission during the review period. A statement of withdrawal must be made in writing to the address listed in § 725.25(c). The withdrawal is effective upon receipt of the statement by the Document Control Officer.

(b) If a manufacturer or importer who withdrew a submission later resubmits a submission for the same microorganism, a new review period begins.

**§ 725.65 Recordkeeping.**

(a) *General provisions*. (1) Any person who files under this part must retain documentation of information in the submission, including (i) any data in the submitter's possession or control; and (ii) records of production volume for the first 3 years of manufacture, import, or processing.

(2) Any person who files under this part must retain documentation of the date of commencement of testing, manufacture, import, or processing.

(3) Any person who is exempt from some or all of the reporting requirements of this part must retain documentation that supports the exemption.

(4) All information required by this section must be retained for 3 years from the date of commencement of each activity for which records are required under this part.

(b) *Specific requirements*. In addition to the requirements of paragraph (a) of this section, specific recordkeeping requirements included in certain subparts must also be followed.

(1) Additional recordkeeping requirements for activities conducted inside a structure are set forth in § 725.235(h).

(2) Additional recordkeeping requirements for TERAs are set forth in § 725.250(f).

(3) Additional recordkeeping requirements for TMEs are set forth in § 725.350(c).

(4) Additional recordkeeping requirements for Tier I exemptions under subpart G of this part are set forth in § 725.424(a)(5).

(5) Additional recordkeeping requirements for Tier II exemptions under subpart G of this part are set forth in § 725.450(d).

(6) Additional recordkeeping requirements for significant new uses of microorganisms reported under subpart L of this part are set forth in § 725.850. Recordkeeping requirements may also be included when a microorganism and significant new use are added to subpart M of this part.

**§ 725.67 Applications to exempt new microorganisms from this part.**

(a) *Submission*. (1) Any manufacturer or importer of a new microorganism may request, under TSCA section 5(h)(4), an exemption, in whole or in part, from this part by sending a Letter of Application to the Director, Chemical Control Division, Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency, 401 M St., SW., Washington, DC 20460.

(2) The Letter of Application should provide information to show that any activities affected by the requested exemption will not present an unreasonable risk of injury to health or the environment. This information should include data described in the following paragraphs.

(i) The effects of the new microorganism on health and the environment.

(ii) The magnitude of exposure of human beings and the environment to the new microorganism.

(iii) The benefits of the new microorganism for various uses and the availability of substitutes for such uses.

(iv) The reasonably ascertainable economic consequences of granting or denying the exemption, including effects on the national economy, small business, and technological innovation.

(b) *Processing of the Letter of Application by EPA*—(1) *Grant of the Application*. If, after consideration of the Letter of Application and any other relevant information available to the Agency, the Assistant Administrator for Prevention, Pesticides and Toxic Substances makes a preliminary determination that the new microorganism will not present an unreasonable risk of injury to health or the environment, the Assistant Administrator will propose a rule to grant the exemption using the applicable procedures in part 750 of this chapter.

(2) *Denial of the application*. If the Assistant Administrator decides that the preliminary determination described in paragraph (b)(1) of this section cannot be made, the application will be denied by sending the applicant a written statement with the Assistant Administrator's reasons for denial.

(c) *Processing of the exemption*—(1) *Unreasonable risk standard*. Granting a TSCA section 5(h)(4) exemption requires a determination that there will be no unreasonable risk.

(i) An unreasonable risk determination under TSCA is an administrative judgment that requires balancing of the harm to health or the environment that a chemical substance may cause and the magnitude and severity of that harm, against the social and economic effects on society of Agency action to reduce that harm.

(ii) A determination of unreasonable risk under TSCA section 5(h)(4) will examine the

reasonably ascertainable economic and social consequences of granting or denying the exemption after consideration of the effect on the national economy, small business, technological innovation, the environment, and public health.

(2) *Grant of the exemption*. The exemption will be granted if the Assistant Administrator determines, after consideration of all relevant evidence presented in the rulemaking proceeding described in paragraph (b)(1) of this section, that the new microorganism will not present an unreasonable risk of injury to health or the environment.

(3) *Denial of the exemption*. The exemption will be denied if the Assistant Administrator determines, after consideration of all relevant evidence presented in the rulemaking proceeding described in paragraph (b)(1) of this section, that the determination described in paragraph (c)(2) of this section cannot be made. A final decision terminating the rulemaking proceeding will be published in the **Federal Register**.

### § 725.70 Compliance.

(a) Failure to comply with any provision of this part is a violation of section 15 of the Act (15 U.S.C. 2614).

(b) A person who manufactures or imports a microorganism before a MCAN is submitted and the MCAN review period expires is in violation of section 15 of the Act even if that person was not required to submit the MCAN under § 725.105.

(c) Using a microorganism which a person knew or had reason to know was manufactured, processed, or distributed in commerce in violation of section 5 of the Act or this part is a violation of section 15 of the Act (15 U.S.C. 2614).

(d) Failure or refusal to establish and maintain records or to permit access to or copying of records, as required by the Act, is a violation of section 15 of the Act (15 U.S.C. 2614).

(e) Failure or refusal to permit entry or inspection as required by section 11 of the Act is a violation of section 15 of the Act (15 U.S.C. 2614).

(f) Violators may be subject to the civil and criminal penalties in section 16 of the Act (15 U.S.C. 2615) for each violation. Persons who submit materially misleading or false information in connection with the requirements of any provision of this part may be subject to penalties calculated as if they never filed their submissions.

(g) EPA may seek to enjoin the manufacture or processing of a microorganism in violation of this part or act to seize any microorganism manufactured or processed in violation of this part or take other actions under the authority of section 7 of the Act (15 U.S.C. 2606) or section 17 of the Act (15 U.S.C. 2616).

### § 725.75 Inspections.

EPA will conduct inspections under section 11 of the Act to assure compliance with section 5 of the Act and this part, to verify that information required by EPA under this part is true and correct, and to audit data submitted to EPA under this part.

## Subpart C—Confidentiality and Public Access to Information

### § 725.80 General provisions for confidentiality claims.

(a) A person may assert a claim of confidentiality for any information submitted to EPA under this part.

(1) Any person who asserts a claim of confidentiality for portions of the specific microorganism identity must provide the information as described in § 725.85.

(2) Any person who asserts a claim of confidentiality for a use of a microorganism must provide the information as described in § 725.88.

(3) Any person who asserts a claim of confidentiality for information contained in a health and safety study of a microorganism must provide the information described in § 725.92.

(b) Any claim of confidentiality must accompany the information when it is submitted to EPA.

(1) When a person submits any information under this part, including any attachments, the claim(s) must be asserted by circling the specific information which is claimed as confidential and marking the page on which that information appears with an appropriate designation such as ''trade secret,'' ''TSCA CBI,'' or ''confidential business information.''

(2) If any information is claimed confidential, the person must submit two copies of the information.

(i) One copy of the information must be complete. In that copy, the submitter must mark the information which is claimed as confidential in the manner prescribed in paragraph (b)(1) of this section.

(ii) The second copy must be complete except that all information claimed as confidential in the first copy must be deleted. EPA will place the second copy in the public file.

(iii) If the submitter does not provide the second copy, the submission is incomplete and the review period does not begin to run until EPA receives the second copy, in accordance with § 725.33.

(iv) Any information contained within the copy submitted under paragraph (b)(2)(ii) of this section which has been in the public file for more than 30 days will be presumed to be in the public domain, notwithstanding any assertion of confidentiality made under this section.

(c) Any person asserting a claim of confidentiality under this part must substantiate each claim in accordance with the requirements in § 725.94.

(d) EPA will disclose information that is subject to a claim of confidentiality asserted under this section only to the extent permitted by the Act, this subpart, and part 2 of this title.

(e) If a submitter does not assert a claim of confidentiality for information at the time it is submitted to EPA, EPA may make the information public and place it in the public file without further notice to the submitter.

### § 725.85 Microorganism identity.

(a) *Claims applicable to the period prior to commencement of manufacture or import for general*

*commercial use*—(1) *When to make a claim.* (i) A person who submits information to EPA under this part may assert a claim of confidentiality for portions of the specific microorganism identity at the time of submission of the information. This claim will apply only to the period prior to the commencement of manufacture or import for general commercial use.

(ii) A person who submits information to EPA under this part must reassert a claim of confidentiality and substantiate the claim each time the information is submitted to EPA. If a person claims certain information confidential in a TERA submission and wishes the same information to remain confidential in a subsequent TERA or MCAN submission, the person must reassert and resubstantiate the claim in the subsequent submission.

(2) *Assertion of claim.* (i) A submitter may assert a claim of confidentiality only if the submitter believes that public disclosure prior to commencement of manufacture or import for general commercial use of the fact that anyone is initiating research and development activities pertaining to the specific microorganism or intends to manufacture or import the specific microorganism for general commercial use would reveal confidential business information. Claims must be substantiated in accordance with the requirements of § 725.94(a).

(ii) If the submission includes a health and safety study concerning the microorganism and if the claim for confidentiality with respect to the specific identity is denied in accordance with § 725.92(c), EPA will deny a claim asserted under paragraph (a) of this section.

(3) *Development of generic name.* Any person who asserts a claim of confidentiality for portions of the specific microorganism identity under this paragraph must provide one of the following items at the time the submission is filed:

(i) The generic name which was accepted by EPA in the prenotice consultation conducted under paragraph (a)(4) of this section.

(ii) One generic name that is only as generic as necessary to protect the confidential identity of the particular microorganism. The name should reveal the specific identity to the maximum extent possible. The generic name will be subject to EPA review and approval.

(4) *Determination by EPA.* (i) Any person who intends to assert a claim of confidentiality for the specific identity of a new microorganism may seek a determination by EPA of an appropriate generic name for the microorganism before filing a submission. For this purpose, the person should submit to EPA:

(A) The specific identity of the microorganism.

(B) A proposed generic name(s) which is only as generic as necessary to protect the confidential identity of the new microorganism. The name(s) should reveal the specific identity of the microorganism to the maximum extent possible.

(ii) Within 30 days, EPA will inform the submitter either that one of the proposed generic names is adequate or that none is adequate and further consultation is necessary.

(5) *Use of generic name.* If a submitter claims microorganism identity as confidential under paragraph (a) of this section, and if the submitter complies with paragraph (a)(2) of this section, EPA will issue for publication in the **Federal Register** notice described in § 725.40 the generic name proposed by the submitter or one agreed upon by EPA and the submitter.

(b) *Claims applicable to the period after commencement of manufacture or import for general commercial use*—(1) *Maintaining claim.* Any claim of confidentiality under paragraph (a) of this section is applicable only until the microorganism is manufactured or imported for general commercial use and becomes eligible for inclusion on the Inventory. To maintain the confidential status of the microorganism identity when the microorganism is added to the Inventory, a submitter must reassert the confidentiality claim and substantiate the claim in the notice of commencement of manufacture required under § 725.190.

(i) A submitter may not claim the microorganism identity confidential for the period after commencement of manufacture or import for general commercial use unless the submitter claimed the microorganism identity confidential under paragraph (a) of this section in the MCAN submitted for the microorganism.

(ii) A submitter may claim the microorganism identity confidential for the period after commencement of manufacture or import for general commercial use if the submitter did not claim the microorganism identity confidential under paragraph (a) of this section in any TERA submitted for the microorganism, but subsequently did claim microorganism identity confidential in the MCAN submitted for the microorganism.

(2) *Assertion of claim.* (i) A person who believes that public disclosure of the fact that anyone manufactures or imports the microorganism for general commercial use would reveal confidential business information may assert a claim of confidentiality under paragraph (b) of this section.

(ii) If the notice includes a health and safety study concerning the new microorganism, and if the claim for confidentiality with respect to the microorganism identity is denied in accordance with § 725.92(c), EPA will deny a claim asserted under paragraph (b) of this section.

(3) *Requirements for assertion.* Any person who asserts a confidentiality claim for microorganism identity must:

(i) Comply with the requirements of paragraph (a)(3) of this section regarding submission of a generic name.

(ii) Agree that EPA may disclose to a person with a *bona fide* intent to manufacture or import the microorganism the fact that the particular microorganism is included on the confidential Inventory for

purposes of notification under section 5(a)(1)(A) of the Act.

(iii) Have available and agree to furnish to EPA upon request the taxonomic designations and supplemental information required by § 725.12.

(iv) Provide a detailed written substantiation of the claim, in accordance with the requirements of § 725.94(b).

(4) *Denial of claim.* If the submitter does not meet the requirements of paragraph (b) of this section, EPA will deny the claim of confidentiality.

(5) *Acceptance of claim.* (i) EPA will publish a generic name on the public Inventory if:

(A) The submitter asserts a claim of confidentiality in accordance with this paragraph.

(B) No claim for confidentiality of the microorganism identity as part of a health and safety study has been denied in accordance with part 2 of this title or § 725.92.

(ii) Publication of a generic name on the public Inventory does not create a category for purposes of the Inventory. Any person who has a bona fide intent to manufacture or import a microorganism which is described by a generic name on the public Inventory may submit an inquiry to EPA under § 725.15(b) to determine whether the particular microorganism is included on the confidential Inventory.

(iii) Upon receipt of a request described in § 725.15(b), EPA may require the submitter who originally asserted confidentiality for a microorganism to submit to EPA the information listed in paragraph (b)(3)(iii) of this section.

(iv) Failure to submit any of the information required under paragraph (b)(3)(iii) of this section within 10 calendar days of receipt of a request by EPA under paragraph (b) of this section will constitute a waiver of the original submitter's confidentiality claim. In this event, EPA may place the specific microorganism identity on the public Inventory without further notice to the original submitter.

(6) *Use of generic name on the public Inventory.* If a submitter asserts a claim of confidentiality under paragraph (b) of this section, EPA will examine the generic microorganism name proposed by the submitter.

(i) If EPA determines that the generic name proposed by the submitter is only as generic as necessary to protect the confidential identity of the particular microorganism, EPA will place that generic name on the public Inventory.

(ii) If EPA determines that the generic name proposed by the submitter is more generic than necessary to protect the confidential identity, EPA will propose in writing, for review by the submitter, an alternative generic name that will reveal the identity of the microorganism to the maximum extent possible.

(iii) If the generic name proposed by EPA is acceptable to the submitter, EPA will place that generic name on the public Inventory.

(iv) If the generic name proposed by EPA is not acceptable to the submitter, the submitter must explain in detail why disclosure of that generic name would reveal confidential business information and propose another generic name which is only as generic as necessary to protect the confidential identity of the microorganism. If EPA does not receive a response from the submitter within 30 days after the submitter receives the proposed name, EPA will place EPA's chosen generic name on the public Inventory. If the submitter does provide the information requested, EPA will review the response. If the submitter's proposed generic name is acceptable, EPA will publish that generic name on the public Inventory. If the submitter's proposed generic name is not acceptable, EPA will notify the submitter of EPA's choice of a generic name. Thirty days after this notification, EPA will place the chosen generic name on the public Inventory.

### § 725.88 Uses of a microorganism.

(a) *Assertion of claim.* A person who submits information to EPA under this part on the categories or proposed categories of use of a microorganism may assert a claim of confidentiality for this information.

(b) *Requirements for claim.* A submitter that asserts such a claim must:

(1) Report the categories or proposed categories of use of the microorganism.

(2) Provide, in nonconfidential form, a description of the uses that is only as generic as necessary to protect the confidential business information. The generic use description will be included in the **Federal Register** notice described in § 725.40.

(c) *Generic use description.* The person must submit the information required by paragraph (b) of this section by describing the uses as precisely as possible, without revealing the information which is claimed confidential, to disclose as much as possible how the use may result in human exposure to the microorganism or its release to the environment.

### § 725.92 Data from health and safety studies of microorganisms.

(a) *Information other than specific microorganism identity*. Except as provided in paragraph (b) of this section, EPA will deny any claim of confidentiality with respect to information included in a health and safety study of a microorganism, unless the information would disclose confidential business information concerning:

(1) Processes used in the manufacture or processing of a microorganism.

(2) Information which is not in any way related to the effects of a microorganism on human health or the environment, such as, the name of the submitting company, cost or other financial data, product development or marketing plans, and

advertising plans, for which the person submits a claim of confidentiality in accordance with § 725.80.

(b) *Microorganism identity*—(1) *Claims applicable to the period prior to commencement of manufacture or import for general commercial use*. A claim of confidentiality for the period prior to commencement of manufacture or import for general commercial use for the specific identity of a microorganism for which a health and safety study was submitted must be asserted in conjunction with a claim asserted under § 725.85(a). The submitter must substantiate each claim in accordance with the requirements of § 725.94(a).

(2) *Claims applicable to the period after commencement of manufacture or import for general commercial use*. To maintain the confidential status of the specific identity of a microorganism for which a health and safety study was submitted after commencement of manufacture or import for general commercial use, the claim must be reasserted and substantiated in conjunction with a claim under § 725.85(b). The submitter must substantiate each claim in accordance with the requirements of § 725.94(b).

(c) *Denial of confidentiality claim*. EPA will deny a claim of confidentiality for microorganism identity under paragraph (b) of this section, unless:

(1) The information would disclose processes used in the manufacture or processing of a microorganism.

(2) The microorganism identity is not necessary to interpret a health and safety study.

(d) *Use of generic names*. When EPA discloses a health and safety study containing a microorganism identity, which the submitter has claimed confidential, and if the Agency has not denied the claim under paragraph (c) of this section, EPA will identify the microorganism by the generic name selected under § 725.85.

**§ 725.94 Substantiation requirements.**

(a) *Claims applicable to the period prior to commencement of manufacture or import for general commercial use*—(1) *MCAN, TME, Tier I certification, and Tier II exemption request requirements*. Any person who submits a MCAN, TME, Tier I certification, or Tier II exemption request should strictly limit confidentiality claims to that information which is confidential and proprietary to the business.

(i) If any information in the submission is claimed as confidential business information, the submitter must substantiate each claim by submitting written answers to the questions in paragraphs (c), (d), and (e) of this section at the time the person submits the information.

(ii) If the submitter does not provide written substantiation as required in paragraph (a)(1)(i) of this section, the submission will be considered incomplete and the review period will not begin in accordance with § 725.33.

(2) *TERA requirements*. Any person who submits a TERA, should strictly limit confidentiality claims to that information which is confidential and proprietary to the business.

(i) If any information in such a submission is claimed as confidential business information, the submitter must substantiate each of those claims by submitting written answers to the questions in paragraphs (d) and (e) of this section at the time the person submits the information.

(ii) If the submitter does not provide written substantiation as required in paragraph (a)(2)(i) of this section, the submission will be considered incomplete and the TERA review period will not begin.

(b) *Claims applicable to the period after commencement of manufacture or import for general commercial use*. (1) If a submitter claimed portions of the microorganism identity confidential in the MCAN and wants the identity to be listed on the confidential Inventory, the claim must be reasserted and substantiated at the time the Notice of Commencement (NOC) is submitted. Otherwise, EPA will list the specific microorganism identity on the public Inventory.

(2) The submitter must substantiate the claim for confidentiality of the microorganism identity by answering all of the questions in paragraphs (c), (d), and (e) in this section. In addition, the following questions must be answered:

(i) What harmful effects to the company or institution's competitive position, if any, would result if EPA publishes on the Inventory the identity of the microorganism? How could a competitor use such information given the fact that the identity of the microorganism otherwise would appear on the TSCA Inventory with no link between the microorganism and the company or industry? How substantial would the harmful effects of disclosure be? What is the causal relationship between the disclosure and the harmful effects?

(ii) Has the identity of the microorganism been kept confidential to the extent that competitors do not know it is being manufactured or imported for general commercial use by anyone?

(c) *General questions*. The following questions must be answered in detail for each confidentiality claim:

(1) For what period of time is a claim of confidentiality being asserted? If the claim is to extend until a certain event or point in time, indicate that event or time period. Explain why the information should remain confidential until such point.

(2) Briefly describe any physical or procedural restrictions within the company or institution relating to the use and storage of the information claimed as confidential. What other steps, if any, apply to use or further disclosure of the information?

(3) Has the information claimed as confidential been disclosed to individuals outside of the company or institution? Will it be disclosed to such persons in the future? If so, what restrictions, if any, apply to use

or further disclosure of the information?

(4) Does the information claimed as confidential appear, or is it referred to, in any of the following:

(i) Advertising or promotional materials for the microorganism or the resulting end product.

(ii) Material safety data sheets or other similar materials for the microorganism or the resulting end product.

(iii) Professional or trade publications.

(iv) Any other media available to the public or to your competitors.

(v) Patents.

(vi) Local, State, or Federal agency public files.

If the answer is yes to any of these questions, indicate where the information appears and explain why it should nonetheless be treated as confidential.

(5) Has EPA, another Federal agency, a Federal court, or a State made any confidentiality determination regarding the information claimed as confidential? If so, provide copies of such determinations.

(6) For each type of information claimed confidential, describe the harm to the company or institution's competitive position that would result if this information were disclosed. Why would this harm be substantial? How could a competitor use such information? What is the causal connection between the disclosure and harm?

(7) If EPA disclosed to the public the information claimed as confidential, how difficult would it be for the competitor to enter the market for the resulting product? Consider such constraints as capital and marketing cost, specialized technical expertise, or unusual processes.

(d) *Microorganism identity and production method*. If confidentiality claims are asserted for the identity of the microorganism or information on how the microorganism is produced, the following questions must be answered:

(1) Has the microorganism or method of production been patented in the U.S. or elsewhere? If so, why is confidentiality necessary?

(2) Does the microorganism leave the site of production or testing in a form which is accessible to the public or to competitors? What is the cost to a competitor, in time and money, to develop appropriate use conditions? What factors facilitate or impede product analysis?

(3) For each additional type of information claimed as confidential, explain what harm would result from disclosure of each type of information if the identity of the microorganism were to remain confidential.

(e) *Health and safety studies of microorganisms*. If confidentiality claims are asserted for information in a health or safety study of a microorganism, the following questions must be answered:

(1) Would the disclosure of the information claimed confidential reveal: (i) Confidential process information, or (ii) information unrelated to the effects of the microorganism on human health and the environment. Describe the causal connection between the disclosure and harm.

(2) Does the company or institution assert that disclosure of the microorganism identity is not necessary to interpret any health and safety studies which have been submitted? If so, explain how a less specific identity would be sufficient to interpret the studies.

### § 725.95 Public file.

All information submitted, including any health and safety study of a microorganism and other supporting documentation, will become part of the public file for that submission, unless such materials are claimed confidential. In addition, EPA may add materials to the public file, unless such materials are claimed confidential. Any of the nonconfidential material described in this subpart will be available for public inspection in the TSCA Public Docket Office, Rm. NE–B607, 401 M St., SW., Washington, DC, between the hours of 8 a.m. and noon and 1 p.m. to 4 p.m., Monday through Friday, excluding legal holidays.

## Subpart D—Microbial Commercial Activities Notification Requirements

### § 725.100 Scope and purpose.

(a) This subpart establishes procedures for submission of a notice to EPA under section 5(a) of TSCA for persons who manufacture, import, or process microorganisms for commercial purposes. This notice is called a Microbial Commercial Activity Notice (MCAN). It is expected that MCANs will in general only be submitted for microorganisms intended for general commercial use.

(b) Persons subject to MCAN submission are described in § 725.105.

(c) Exclusions and exemptions specific to MCAN submissions are described in § 725.110.

(d) Submission requirements applicable specifically to MCANs are described at § 725.150.

(e) Data requirements for MCANs are set forth in § § 725.155 and 725.160.

(f) EPA review procedures specific to MCANs are set forth in § 725.170.

(g) Subparts A through C of this part apply to any MCAN submitted under this subpart.

### § 725.105 Persons who must report.

(a) *Manufacturers of new microorganisms*. (1) MCAN submission is required for any person who intends to manufacture for general commercial use in the United States a new microorganism. Exclusions are described in § 725.110.

(2) If a person contracts with a manufacturer to produce or process a new microorganism and (i) The manufacturer produces or processes the microorganism exclusively for that person, and (ii) that person specifies the identity of the microorganism, and controls the total amount produced and the basic technology for the plant process, then that person must submit the MCAN.

If it is unclear who must report, EPA should be contacted to determine who must submit the MCAN.

(3) Only manufacturers that are incorporated, licensed, or doing business in the United States may submit a MCAN.

(b) *Importers of new microorganisms*. (1) MCAN submission is required for a person who intends to import into the United States for general commercial use a new microorganism. Exclusions are described in § 725.110.

(2) When several persons are involved in an import transaction, the MCAN must be submitted by the principal importer. If no one person fits the principal importer definition in a particular transaction, the importer should contact EPA to determine who must submit the MCAN for that transaction.

(3) Except as otherwise provided in paragraph (b)(4) of this section, the provisions of this subpart D apply to each person who submits a MCAN for a new microorganism which such person intends to import for a general commercial use. In addition, each importer must comply with paragraph (b)(4) of this section.

(4) EPA will hold the principal importer, or the importer that EPA determines must submit the MCAN when there is no principal importer under paragraph (b)(2) of this section, liable for complying with this part, for completing the MCAN, and for the completeness and truthfulness of all information which it submits.

(c) *Manufacturers, importers, or processors of microorganisms who intend to use or distribute the microorganism for a significant new use*. MCAN submission is required for any person who intends to manufacture, import, or process for commercial purposes a microorganism identified as having one or more significant new uses in subpart M of this part, and who intends either to engage in a significant new use of the microorganism or intends to distribute it in commerce. Persons excluded from reporting on significant new uses of microorganisms and additional procedures for reporting are described in subpart L of this part.

### § 725.110 Persons not subject to this subpart.

Persons are not subject to the requirements of this subpart for the following activities:

(a) Manufacturing, importing, or processing solely for research and development microorganisms that meet the requirements for an exemption under subpart E of this part.

(b) Manufacturing, importing, or processing microorganisms for test marketing activities which have been granted an exemption under subpart F of this part.

(c) Manufacturing or importing microorganisms under the conditions of a Tier I or Tier II exemption under subpart G of this part.

### § 725.150 Procedural requirements for this subpart.

General requirements for all MCANs under this part are contained in § 725.25. In addition, the following requirements apply to MCANs submitted under this subpart:

(a) *When to submit a MCAN*. A MCAN must be submitted at least 90 calendar days prior to manufacturing or importing a new microorganism and at least 90 calendar days prior to manufacturing, importing, or processing a microorganism for a significant new use.

(b) *Section 5(b) of TSCA*. The submitter must comply with any applicable requirement of section 5(b) of TSCA.

(c) *Contents of a MCAN*. Each person who submits a MCAN under this subpart must provide the information and test data described in § § 725.155 and 725.160.

(d) *Recordkeeping*. Each person who submits a MCAN under this subpart must comply with the recordkeeping requirements of § 725.65.

### § 725.155 Information to be included in the MCAN.

(a) Each person who is required by this part to submit a MCAN must provide EPA in writing with all information known to or reasonably ascertainable by the person that would permit EPA to make a reasoned evaluation of the human health and environmental effects of the microorganism, or any microbial mixture or article, including information on its effects on humans, animals, plants, and other microorganisms, and in the environment. However, no person is required to include information which relates solely to exposure of humans or ecological populations outside of the United States. The information to be submitted under this subpart includes, but is not limited to, the information listed in paragraphs (c) through (h) of this section. All information submitted must be true and correct.

(b) When specific information is not submitted, an explanation of why such information is not available or not applicable must be included.

(c) *Submitter identification*. (1) The name and headquarters address of the submitter.

(2) The name, address, and office telephone number (including area code) of the principal technical contact representing the submitter.

(d) *Microorganism identity information*. Persons must submit sufficient information to allow the microorganism to be accurately and unambiguously identified for listing purposes as required by § 725.12.

(1) *Description of the recipient microorganism(s) and the new microorganism*. (i) Data substantiating the taxonomy of the recipient microorganism(s) and the new microorganism(s) to the level of strain, as appropriate. In lieu of data, EPA will accept a letter from a culture collection substantiating taxonomy, provided EPA, upon request to the submitter, may have access to the data supporting the taxonomic designation.

(ii) Information on the morphological and physiological

features of the new microorganism(s).

(iii) Other specific data by which the new microorganism(s) may be uniquely identified for Inventory purposes.

(2) *Genetic construction of the new microorganism(s).* (i) Data substantiating the taxonomy of the donor organism(s). In lieu of data, EPA will accept a letter from a culture collection substantiating taxonomy, provided EPA, upon request to the submitter, may have access to the data supporting the taxonomic designation.

(ii) Description of the traits for which the new microorganism(s) has been selected or developed and other traits known to have been added or modified.

(iii) A detailed description of the genetic construction of the new microorganism, including the technique used to modify the microorganism (e.g., fusion of cells, injection of DNA, electroporation or chemical poration, or methods used for induced mutation and selection). The description should include, for example, function of the introduced genetic material, including any changes predicted to alter function; how the introduced genetic material is expected to affect behavior; expression, alteration, and stability of the introduced genetic material; methods for vector construction and introduction; and a description of the regulatory and structural genes that are components of the introduced genetic material, including genetic maps of the introduced sequences.

(3) *Phenotypic and ecological characteristics*. (i) Habitat, geographical distribution, and source of the recipient microorganism(s).

(ii) Survival and dissemination under relevant environmental conditions including a description of methods for detecting the microorganism(s) in the environment and the sensitivity limit of detection for these techniques.

(iii) A description of anticipated biological interactions with and effects on target organisms and other organisms such as competitors, prey, hosts, symbionts, parasites, and pathogens; a description of host range; a description of pathogenicity, infectivity, toxicity, virulence, or action as a vector of pathogens; and capacity for genetic transfer under laboratory and relevant environmental conditions.

(iv) A description of anticipated involvement in biogeochemical or biological cycling processes, involvement in rate limiting steps in mineral or nutrient cycling, or involvement in inorganic compounds cycling (such as possible sequestration or transformation of heavy metals).

(e) *Byproducts*. A description of the byproducts resulting from the manufacture, processing, use, and disposal of the new microorganism(s).

(f) *Total production volume*. The estimated maximum amount of the new microorganism(s) intended to be manufactured or imported during the first year of production and the estimated maximum amount to be manufactured or imported during any consecutive 12–month period during the first 3 years of production. This estimate may be by weight or volume and should include an estimation of viability (i.e., viable cells per unit volume or colony forming units per unit dry weight).

(g) *Use information*. A description of intended categories of use by function and application, the estimated percent of production volume devoted to each category of use, and the percent of the new microorganism(s) in the formulation for each commercial or consumer use.

(h) *Worker exposure and environmental release*. (1) For sites controlled by the submitter:

(i) The identity of sites where the new microorganism(s) will be manufactured, processed, or used. For purposes of this section, the site for a person who imports a new microorganism is the site of the operating unit within the person's organization which is directly responsible for importing the new microorganism and which controls the import transaction. The import site may in some cases be the organization's headquarters office in the United States.

(ii) A process description of each manufacture, processing, and use operation, which includes a diagram of the major unit operations and conversions, the identity and entry point of all feedstocks, and the identity of any possible points of release of the new microorganism from the process, including a description of all controls, including engineering controls, used to prevent such releases.

(iii) Worker exposure information, including worker activities, physical form of process streams which contain the new microorganism to which workers may be exposed, the number of workers, and the duration of activities.

(iv) Information on release of the new microorganism to the environment, including the quantity and media of release and type of control technology used.

(v) A narrative description of the intended transport of the new microorganism, including the means of transport, containment methods to be used during transport, and emergency containment procedures to be followed in case of accidental release.

(vi) Procedures for disposal of any articles, waste, clothing, or other equipment involved in the activity, including procedures for inactivation of the new microorganism, containment, disinfection, and disposal of contaminated items.

(2) For sites not controlled by the submitter, a description of each type of processing and use operation involving the new microorganism, including identification of the estimated number of processing or use sites, situations in which worker exposure to and/or environmental release of the new microorganism will occur, the number of workers exposed and the duration of exposure; procedures for transport of the new microorganism and for disposal, including procedures for inactivation of the new

microorganism; and control measures which limit worker exposure and environmental release.

**§ 725.160 Submission of health and environmental effects data.**

(a) *Test data on the new microorganism in the possession or control of the submitter*. (1) Except as provided in § 725.25(h), and in addition to the information required by § 725.155(d)(3), each MCAN must contain all test data in the submitter's possession or control which are related to the effects on health or the environment of any manufacture, processing, distribution in commerce, use, or disposal of the new microorganism or any microbial mixture or article containing the new microorganism, or any combination of such activities. This includes test data concerning the new microorganism in a pure culture or formulated form as used in one of the activities listed above.

(2) A full report or standard literature citation must be submitted for the following types of test data:

(i) Health effects data.

(ii) Ecological effects data.

(iii) Physical and chemical properties data.

(iv) Environmental fate characteristics.

(v) Monitoring data and other test data related to human exposure to or environmental release of the new microorganism.

(3)(i) If the data do not appear in the open scientific literature, the submitter must provide a full report. A full report includes the experimental methods and materials, results, discussion and data analysis, conclusions, references, and the name and address of the laboratory that developed the data.

(ii) If the data appear in the open scientific literature, the submitter need only provide a standard literature citation. A standard literature citation includes author, title, periodical name, date of publication, volume, and page numbers.

(4)(i) If a study, report, or test is incomplete when a person submits a MCAN, the submitter must identify the nature and purpose of the study; name and address of the laboratory developing the data; progress to date; types of data collected, significant preliminary results; and anticipated completion date.

(ii) If a test or experiment is completed before the MCAN review period ends, the person must submit the study, report, or test to the address listed in § 725.25(c), as specified in paragraph (a)(3)(i) of this section, within 10 days of receiving it, but no later than 5 days before the end of the review period. If the test or experiment is completed during the last 5 days of the review period, the submitter must immediately inform its EPA contact for that submission by telephone.

(5) For test data in the submitter's possession or control which are not listed in paragraph (a)(2) of this section, a person is not required to submit a complete report. The person must submit a summary of the data. If EPA so requests, the person must submit a full report within 10 days of the request, but no later than 5 days before the end of the review period.

(6) All test data described under paragraph (a) of this section are subject to these requirements, regardless of their age, quality, or results.

(b) *Other data concerning the health and environmental effects of the new microorganism that are known to or reasonably ascertainable by the submitter*. (1) Except as provided in § 725.25(h), and in addition to the information required by § 725.155(c)(3), any person who submits a MCAN must describe the following data, including any data from a health and safety study of a microorganism, if the data are related to effects on health or the environment of any manufacture, processing, distribution in commerce, use, or disposal of the microorganism, of any microbial mixture or article containing the new microorganism, or of any combination of such activities:

(i) Any data, other than test data, in the submitter's possession or control.

(ii) Any data, including test data, which are not in the submitter's possession or control, but which are known to or reasonably ascertainable by the submitter. For the purposes of this section, data are known to or reasonably ascertainable by the submitter if the data are known to any of its employees or other agents who are associated with the research and development, test marketing, or commercial marketing of the microorganism.

(2) Data that must be described include data concerning the new microorganism in a pure culture or formulated form as used in one of the activities listed in paragraph (b)(1) of this section.

(3) The description of data reported under paragraph (b) of this section must include:

(i) If the data appear in the open scientific literature, a standard literature citation, which includes the author, title, periodical name, date of publication, volume, and pages.

(ii) If the data are not available in the open scientific literature, a description of the type of data and summary of the results, if available, and the names and addresses of persons the submitter believes may have possession or control of the data.

(4) All data described by paragraph (b) of this section are subject to these requirements, regardless of their age, quality, or results; and regardless of whether they are complete at the time the MCAN is submitted.

**§ 725.170 EPA review of the MCAN.**

General procedures for review of all submissions under this part are contained in § § 725.28 through 725.60. In addition, the following procedures apply to EPA review of MCANs submitted under this subpart:

(a) Length of the review period. The MCAN review period specified in section 5(a) of the Act runs for 90 days from the date the Document

Control Officer for the Office of Pollution Prevention and Toxics receives a complete MCAN, or the date EPA determines the MCAN is complete under § 725.33, unless the Agency extends the period under section 5(c) of the Act and § 725.56.

(b) Notice of expiration of MCAN review period. (1) EPA will notify the submitter that the MCAN review period has expired or that EPA has completed its review of the MCAN. Expiration of the review period does not constitute EPA approval or certification of the new microorganism, and does not mean that EPA may not take regulatory action against the microorganism in the future.

(2) After expiration of the MCAN review period, in the absence of regulatory action by EPA under section 5(e), 5(f), or 6(a) of the Act, the submitter may manufacture or import the microorganism even if the submitter has not received notice of expiration.

(3) Early notification that EPA has completed its review does not permit commencement of manufacture or import prior to the expiration of the 90–day MCAN review period.

(c) Any person submitting a MCAN in response to the requirements of this subpart shall not manufacture, import, or process a microorganism subject to this subpart until the review period, including all extensions and suspensions, has expired.

### § 725.190 Notice of commencement of manufacture or import.

(a) *Applicability*. Any person who commences the manufacture or import of a new microorganism for nonexempt, general commercial use for which that person previously submitted a section 5(a) notice under this part must submit a notice of commencement (NOC) of manufacture or import.

(b) *When to report*. (1) If manufacture or import for nonexempt, general commercial use begins on or after [insert date 44 days after date of publication in the **Federal Register** of the final rule], the submitter must submit the NOC to EPA no later than 30 calendar days after the first day of such manufacture or import.

(2) If manufacture or import for nonexempt, general commercial use began or will begin before [insert date 44 days after date of publication in the **Federal Register** of the final rule], the submitter must submit the NOC by [insert date 44 days after date of publication in the **Federal Register** of the final rule].

(3) Submission of an NOC prior to the commencement of manufacture or import is a violation of TSCA section 15.

(c) *Information to be reported*. The NOC must contain the following information: Specific microorganism identity, MCAN number, and the date when manufacture or import commences. If the person claimed microorganism identity confidential in the MCAN, and wants the identity to be listed on the confidential Inventory, the claim must be reasserted and resubstantiated in accordance with § 725.85(b). Otherwise, EPA will list the specific microorganism identity on the public Inventory.

(d) *Where to submit*. NOCs should be submitted to the address listed in § 725.25(c).

## Subpart E—Exemptions for Research and Development Activities

### § 725.200 Scope and purpose.

(a) This subpart describes exemptions from the reporting requirements under subpart D of this part for research and development activities involving microorganisms.

(b) In lieu of complying with subpart D of this part, persons described in § 725.205 may submit a TSCA Experimental Release Application (TERA) for research and development activities involving microorganisms.

(c) Exemptions from part 725 are provided at § § 725.232, 725.234, and 725.238.

(d) Submission requirements specific for TERAs are described at § 725.250.

(e) Data requirements for TERAs are set forth in § § 725.255 and 725.260.

(f) EPA review procedures specific for TERAs are set forth in § § 725.270 and 725.288.

(g) Subparts A through C of this part apply to any submission under this subpart.

### § 725.205 Persons who may report under this subpart.

(a) Certain research and development activities involving microorganisms subject to TSCA jurisdiction are exempt from reporting under this part. A person conducting research and development activities which do not meet the conditions for the exemptions described in § 725.232, 725.234, or 725.238 may report under this subpart.

(b) A person may report under this subpart for the following research and development activities:

(1) A person who intends to manufacture or import for commercial purposes a new microorganism.

(2) A person who intends to manufacture, import, or process for commercial purposes a microorganism identified in subpart M of this part as a significant new use. Additional reporting requirements for significant new uses are described in subpart L of this part.

### § 725.232 Activities subject to the jurisdiction of other Federal programs or agencies.

This part does not apply to any research and development activity that meets all of the following conditions.

(a) Meets the requirements of § 725.234(a) and (c).

(b) Is receiving research funds from another Federal agency which controls the research in accordance with applicable portions of the NIH ''Guidelines for Research Involving Recombinant DNA Molecules.'' This control may be exercised through direct regulatory authority or through requiring compliance with the NIH

Guidelines as a condition of receiving funds.

### § 725.234 Activities conducted inside a structure.

A person who manufactures, imports, or processes a microorganism is not subject to the reporting requirements under subpart D of this part if all of the following conditions are met:

(a) The microorganism is manufactured, imported, or processed solely for research and development activities.

(b) The microorganism is used by, or directly under the supervision of, a technically qualified individual, as defined in § 725.3. The technically qualified individual must maintain documentation of the procedures selected to comply with paragraph (d) of this section and must ensure that the procedures are used.

(c) There is no intentional testing of a microorganism outside of a structure, as structure is defined in § 725.3.

(d) Containment and/or inactivation controls. (1) Selection and use of containment and/or inactivation controls inside a structure for a particular microorganism shall take into account the following:

(i) Factors relevant to the organism's ability to survive in the environment.

(ii) Potential routes of release in air, solids and liquids; in or on waste materials and equipment; in or on people, including maintenance and custodial personnel; and in or on other organisms, such as insects and rodents.

(iii) Procedures for transfer of materials between facilities.

(2) The TQI's selection of containment and/or inactivation controls shall be approved and certified by an authorized official (other than the TQI) of the institution that is conducting the test prior to the commencement of the test.

(3) Records shall be developed and maintained describing the selection and use of the containment and/or inactivation controls, including contingency plans for emergency clean-up or test termination, that will be used during the test. These records, which must be maintained at the location where the research and development activity is being conducted, shall be submitted to the Agency at the Agency's written request and within the time frame specified in the Agency's request.

(4) Subsequent to Agency review of records in accordance with paragraph (d)(3) of this section, changes to the containment/inactivation controls selected under paragraph (d)(1) of this section must be made upon Agency order. Failure to comply with the Agency's order shall result in automatic loss of eligibility for an exemption under this section.

(e) The manufacturer, importer, or processor notifies all persons in its employ or to whom it directly distributes the microorganism, who are engaged in experimentation, research, or analysis on the microorganism, including the manufacture, processing, use, transport, storage, and disposal of the microorganism associated with research and development activities, of any risk to health, identified under § 725.235(a), which may be associated with the microorganism. The notification must be made in accordance with § 725.235(b).

### § 725.235 Conditions of exemption for activities conducted inside a structure.

(a) *Determination of risks.* (1) To determine whether notification under § 725.234(e) is required, the manufacturer, importer, or processor must review and evaluate the following information to determine whether there is reason to believe there is any risk to health which may be associated with the microorganism:

(i) Information in its possession or control concerning any significant adverse reaction of persons exposed to the microorganism which may reasonably be associated with such exposure.

(ii) Information provided to the manufacturer, importer, or processor by a supplier or any other person concerning a health risk believed to be associated with the microorganism.

(iii) Health and environmental effects data in its possession or control concerning the microorganism.

(iv) Information on health effects which accompanies any EPA rule or order issued under section 4, 5, or 6 of the Act that applies to the microorganism and of which the manufacturer, importer, or processor has knowledge.

(2) When the research and development activity is conducted solely inside a laboratory and exposure to the microorganism is controlled through the implementation of prudent practices for handling microorganisms of unknown human health or environmental effects and any distribution, except for purposes of disposal, is to other such laboratories for further research and development activity, the information specified in paragraph (a)(1) of this section need not be reviewed and evaluated. (For purposes of this paragraph (a)(2), a laboratory is defined as a contained research facility, where relatively small quantities of microorganisms are used on a non-production basis, and where activities involve the use of containers for reactions, transfers, and other handling of microorganisms designed to be easily manipulated by a single individual.)

(b) *Notification to employees.* (1) The manufacturer, importer, or processor must notify the persons identified in § 725.234(e) by means of a container labeling system, conspicuous placement of notices in areas where exposure may occur, written notification to each person potentially exposed, or any other method of notification which adequately informs persons of health risks which the manufacturer, importer, or processor has reason to believe may be associated with the microorganism, as determined under paragraph (a)(1) of this section.

(2) If the manufacturer, importer, or processor distributes a

microorganism manufactured, imported, or processed under this section to persons not in its employ, the manufacturer, importer, or processor must in written form:

(i) Notify those persons that the microorganism is to be used only for research and development purposes.

(ii) Provide the notice of health risks specified in paragraph (b)(1) of this section.

(3) The adequacy of any notification under this section is the responsibility of the manufacturer, importer, or processor.

(c) *No applicability to general commercial use*. A microorganism is not exempt from reporting under subpart D of this part if any amount of the microorganism, including as part of a mixture, is processed, distributed in commerce, or used, for any commercial purpose other than research and development, except where the microorganism is processed, distributed in commerce, or used only as an impurity or as part of an article.

(d) *Waste disposal*. Quantities of the inactivated microorganism, or mixtures or articles containing the inactivated microorganism, remaining after completion of research and development activities may be disposed of as a waste in accordance with applicable Federal, State, and local regulations.

(e) *Impurities and articles*. Quantities of research and development microorganisms existing solely as impurities in a product or incorporated into an article, in accordance with paragraph (c) of this section, are not subject to the requirements of § 725.234 and paragraphs (a) and (b) of this section, once research and development activities have been completed.

(f) *Pesticide uses*. A person who manufactures, imports, or processes a microorganism solely for research and development is not required to comply with the requirements of this section if the person's exclusive intention is to perform research and development activities solely for the purpose of determining whether the microorganism can be used as a pesticide.

(g) *Recordkeeping*. A person who manufactures, imports, or processes a microorganism under this section must retain the following records:

(1) Records describing selection and use of containment and/or inactivation controls required by § 725.234(d)(3) and certification by an authorized official required by § 725.234(d)(2) for each microorganism.

(2) Copies or citations to information reviewed and evaluated under paragraph (a)(1) of this section to determine the need to make any notification of risk.

(3) Documentation of prudent laboratory practices used instead of notification and evaluation under paragraph (a)(2) of this section.

(4) Documentation of the nature and method of notification under paragraph (b)(1) of this section, including copies of any labels or written notices used.

(5) The names and addresses of any persons other than the manufacturer, importer, or processor to whom the substance is distributed, the identity of the microorganism, the amount distributed, and copies of the notifications required under paragraph (b)(2) of this section.

### § 725.238 Activities conducted outside a structure.

(a) *Exemption*. (1) Research and development activities involving intentional testing in the environment of certain microorganisms listed in § 725.239 may be conducted without prior review by EPA if all of the conditions of this section and § 725.239 are met.

(2) The research and development activity involving a microorganism listed in § 725.239 must be conducted by, or directly under the supervision of, a technically qualified individual, as defined in § 725.3.

(b) *Certification*. To be eligible for the exemption under this section, a manufacturer or importer must submit to EPA prior to initiation of the activity a document signed by an authorized official containing the following information:

(1) Name, address, and phone number of the manufacturer or importer.

(2) Location, estimated duration, and planned start date of the test.

(3) Certification of the following:

(i) Compliance with the conditions of the exemption specified for the microorganism in § 725.239.

(ii) Notification of the appropriate Federal and state authorities of the planned test.

(c) *Recordkeeping*. Persons who conduct research and development activities under this section must comply with the recordkeeping requirements of § 725.65 and retain documentation that supports their compliance with the requirements of this section and the specific requirements for the microorganism listed in § 725.239.

### § 725.239 Use of specific microorganisms in activities conducted outside a structure.

(a) *Bradyrhizobium japonicum*. To qualify for an exemption under this section, all of the following conditions must be met for a test involving *Bradyrhizobium japonicum*:

(1) *Characteristics of recipient microorganism*. The recipient microorganism is limited to strains of *Bradyrhizobium japonicum*.

(2) *Modification of traits*. (i) The introduced genetic material must meet the criteria for poorly mobilizable listed in § 725.421(c).

(ii) The introduced genetic material must consist only of the following components:

(A) The structural gene(s) of interest, which have the following limitations:

(*1*) For antibiotic resistance, the structural gene may originate from any source.

(*2*) For traits other than antibiotic resistance, the structural gene must be limited to the genera *Bradyrhizobium* and *Rhizobium*.

(B) The regulatory sequences permitting the expression of solely the gene(s) of interest.

(C) Associated nucleotide sequences needed to move genetic material, including linkers, homopolymers, adaptors,

transposons, insertion sequences, and restriction enzyme sites.

(D) The vector nucleotide sequences needed for vector transfer.

(E) The vector nucleotide sequences needed for vector maintenance.

(3) *Limitations on exposure*. (i) The test site area must be no more than 5 terrestrial acres.

(ii) The technically qualified individual must select appropriate methods to limit the dissemination of modified *Bradyrhizobium japonicum*.

(b) *Rhizobium meliloti*. To qualify for an exemption under this section, all of the following conditions must be met for a test involving *Rhizobium meliloti*:

(1) *Characteristics of recipient microorganism*. The recipient microorganism is limited to strains of *Rhizobium meliloti*.

(2) *Modification of traits*. (i) The introduced genetic material must meet the criteria for poorly mobilizable listed in § 725.421(c) of this part.

(ii) The introduced genetic material must consist only of the following components:

(A) The structural gene(s) of interest, which have the following limitations:

(*1*) For antibiotic resistance, the structural gene may originate from any source.

(*2*) For traits other than antibiotic resistance, the structural gene must be limited to the genera *Bradyrhizobium* and *Rhizobium*.

(B) The regulatory sequences permitting the expression of solely the gene(s) of interest.

(C) Associated nucleotide sequences needed to move genetic material, including linkers, homopolymers, adaptors, transposons, insertion sequences, and restriction enzyme sites.

(D) The vector nucleotide sequences needed for vector transfer.

(E) The vector nucleotide sequences needed for vector maintenance.

(3) *Limitations on exposure*. (i) The test site area must be no more than 5 terrestrial acres.

(ii) The technically qualified individual must select appropriate methods to limit the dissemination of modified *Rhizobium meliloti*.

### § 725.250 Procedural requirements for this subpart.

General requirements for all submissions under this part are contained in § 725.25. In addition, the following requirements apply to applications submitted under this subpart:

(a) When to submit the TERA. Each person who is eligible to submit a TERA under this subpart must submit the TERA at least 60 calendar days prior to initiating the proposed research and development activity.

(b) Contents of the TERA. Each person who submits a TERA under this subpart must provide the information and test data described in § § 725.255 and 725.260. In addition, the submitter must supply sufficient information to enable EPA to evaluate the effects of all activities for which approval is requested.

(c) A person described under § 725.205 may submit a TERA for one or more microorganisms and one or more research and development activities, including a research program.

(d) EPA will either approve the TERA, with or without conditions, or disapprove it under procedures established in this subpart.

(e) The manufacturer, importer, or processor who receives a TERA approval must comply with all terms of the approval and remains liable for compliance with all terms, regardless of who conducts the research and development activity. Any person conducting the research and development activity approved under the TERA must comply with all terms of the TERA approval.

(f) Recordkeeping. Persons submitting a TERA must comply with the recordkeeping requirements of § 725.65. In addition, the following requirements apply to TERAs:

(1) Each person submitting a TERA under this part must retain documentation of information contained in the TERA for a period of 3 years from the date that the results of the study are submitted to the Agency.

(2) Summaries of all data, conclusions, and reports resulting from the conduct of the research and development activity under the TERA must be submitted to the EPA address identified in § 725.25(c) within 1 year of the termination of the activity.

### § 725.255 Information to be included in the TERA.

(a) To review a TERA, EPA must have sufficient information to permit a reasoned evaluation of the health and environmental effects of the planned test in the environment. The person seeking EPA approval must submit all information known to or reasonably ascertainable by the submitter on the microorganism and the research and development activity, including information not listed in paragraphs (c), (d), and (e) of this section that the person believes will be useful for EPA's risk assessment. The TERA must be in writing and must include at least the information described in the following paragraphs.

(b) When specific information is not submitted, an explanation of why such information is not available or not applicable must be included.

(c) Persons applying for a TERA, must include the submitter identification and microorganism identity information required for MCANs in § 725.155(c), (d)(1), and (d)(2).

(d) Persons applying for a TERA must submit phenotypic and ecological characteristics information required in § 725.155(d)(3) as it relates directly to the conditions of the proposed research and development activity.

(e) Persons applying for a TERA must also submit the following information about the proposed research and development activity:

(1) *A detailed description of the proposed research and development activity*. (i) The objectives and significance of the activity and a rationale for testing the microorganisms in the environment.

(ii) Number of cells released (including viability per volume if applicable) and the method(s) of application or release.

(iii) Characteristics of the test site(s), including location, geographical, physical, chemical, and biological features, proximity to human habitation or activity, and description of site characteristics that would influence dispersal or confinement.

(iv) Target organisms (if the microorganism(s) to be tested has an intended target), including identification of each target organism and anticipated mechanism and result of interaction.

(v) Planned start date and duration of each activity.

(vi) Evidence that State authorities have been notified.

(2) *Information on monitoring, confinement, mitigation, and emergency termination procedures*. (i) Confinement procedures for the activity, access and security measures, and procedures for routine termination of the activity.

(ii) Mitigation and emergency procedures.

(iii) Measures to detect and control potential adverse effects.

(iv) Name of principal investigator and chief of site personnel responsible for emergency procedures.

(v) Personal protective equipment, engineering controls, and procedures to be followed to minimize dispersion of the microorganism(s) by people, machinery, or equipment.

(vi) Procedures for disposal of any articles, waste, clothing, machinery, or other equipment involved in the experimental release, including methods for inactivation of the microorganism, containment, disinfection, and disposal of contaminated items.

### § 725.260 Submission of health and environmental effects data.

Each TERA must contain all available data concerning actual or potential effects on human health or the environment of the new microorganism that are in the possession or control of the submitter and a description of other data known to or reasonably ascertainable by the submitter that will permit a reasoned evaluation of the planned test in the environment. The data must be reported in the manner described in § 725.160(a)(3) and (b)(3).

### § 725.270 EPA review of the TERA.

General procedures for review of all submissions under this part are contained in § § 725.28 through 725.60. In addition, the following procedures apply to EPA review of applications submitted under this subpart:

(a) *Length of the review period*. (1) The review period for the TERA will be 60 days from the date the Document Control Officer for the Office of Pollution Prevention and Toxics receives a complete TERA, or the date EPA determines the TERA is complete under § 725.33, unless EPA finds good cause for an extension under § 725.56.

(2) A submitter shall not proceed with the research and development activity described in the TERA unless and until EPA provides written approval of the TERA. A submitter may receive early approval if a review is completed in less than 60 days.

(b) *EPA decision regarding proposed TERA activity*. (1) A decision concerning a TERA under this subpart will be made by the Administrator, or a designee.

(2) If EPA determines that the proposed research and development activity for the microorganism does not present an unreasonable risk of injury to human health or the environment, EPA will notify the submitter that the TERA is approved and that the submitter can proceed with the proposed research and development activity described in the TERA.

(3) EPA may include conditions in its approval of the TERA that would be stated in a TERA agreement under paragraph (c) of this section.

(4) If EPA concludes that the proposed research and development activity may present an unreasonable risk of injury to human health or the environment, EPA will deny the TERA and will provide reasons for the denial in writing.

(c) *TERA agreement*. (1) The TERA agreement is legally binding on the TERA submitter and the Agency. The TERA submitter agrees to be bound by the requirements set out in the agreement and also certifies that all data submitted to the Agency is true and correct.

(2) If EPA approves a TERA, the submitter must conduct the research and development activity only as described in the TERA agreement and in accordance with any conditions set forth by EPA in its approval of the TERA agreement.

(3) Any person who fails to comply with any requirement or condition of the TERA agreement shall be in violation of sections 5 and 15 of TSCA and so subject to civil and criminal penalties under section 16 of TSCA.

### § 725.288 Revocation or modification of TERA approval.

(a) *Significant questions about risk*. (1) If, after approval of a TERA under this subpart, EPA receives information which raises significant questions about the Agency's determination that the activity does not present an unreasonable risk of injury to human health or the environment, EPA will notify the submitter in writing of those questions.

(2) The submitter may, within 10 days of receipt of EPA's notice, provide in writing additional information or arguments concerning the significance of the questions and whether EPA should modify or revoke the approval of the TERA.

(3) After considering any such information and arguments, EPA will decide whether to change its determination regarding approval of the TERA.

(i) If EPA determines that it will continue to approve the TERA, it will notify the submitter in writing. In continuing to approve a TERA, EPA may prescribe additional conditions which must be followed by the submitter. In this case, EPA may reserve the right to review the

test data and revoke the TERA approval after some time period.

(ii) If EPA concludes that it can no longer approve the TERA, it will notify the submitter in writing and state its reasons. In that event, the submitter must terminate the research and development activity within 48 hours of receipt of the notice in accordance with directions provided by EPA in the notice.

(b) *Evidence of unreasonable risk.* (1) If, after approval of a TERA under this subpart, EPA receives information which indicates that the proposed research and development activity will present an unreasonable risk of injury to human health or the environment, EPA will notify the submitter in writing and state its reasons.

(2) The submitter must provide additional safeguards or terminate the research and development activity in accordance with directions provided by EPA in the notice.

(3) The submitter may then submit additional information or arguments concerning the matters raised by EPA and whether EPA should modify or revoke the approval of the TERA in accordance with paragraph (a)(2) of this section.

(4) EPA will consider the information and arguments under paragraph (a)(3) of this section.

(5) The submitter may resume the activity only upon written notice from EPA that EPA has approved resumption of the activity. In approving resumption of an activity, EPA may prescribe additional conditions which must be followed by the submitter.

(c) *Modifications.* If, after approval of a TERA under this subpart, the submitter concludes that it is necessary to alter the conduct of the research and development activity in a manner which would result in the activity being different from that described in the TERA agreement and any conditions EPA prescribed in its approval, the submitter must inform the EPA contact for the TERA and may not modify the activity without the approval of EPA.

## Subpart F—Exemptions for Test Marketing

### § 725.300 Scope and purpose.

(a) This subpart describes exemptions from the reporting requirements under subpart D of this part for test marketing activities involving microorganisms.

(b) In lieu of complying with subpart D of this part, persons described in § 725.305 may submit an application for a test marketing exemption (TME).

(c) Submission requirements specific for TME applications are described at § 725.350.

(d) Data requirements for TME applications are set forth in § 725.355.

(e) EPA review procedures specific for TMEs are set forth in § 725.370.

(f) Subparts A through C of this part apply to any submission under this subpart.

### § 725.305 Persons who may report under this subpart.

A person identified in this section may apply for a test marketing exemption. EPA may grant the exemption if the person demonstrates that the microorganism will not present an unreasonable risk of injury to health or the environment as a result of the test marketing. A person may report under this subpart for the following test marketing activities:

(a) A person who intends to manufacture or import for commercial purposes a new microorganism.

(b) A person who intends to manufacture, import, or process for commercial purposes a microorganism identified in subpart M of this part as a significant new use.

### § 725.350 Procedural requirements for this subpart.

General requirements for all submissions under this part are contained in § 725.25. In addition, the following requirements apply to applications submitted under this subpart:

(a) *Prenotice consultation.* EPA strongly suggests that for a TME, the submitter contact the Agency for a prenotice consultation regarding eligibility for a TME.

(b) *When to submit a TME.* Each manufacturer or importer who is eligible to submit a TME under this subpart must submit the TME at least 45 calendar days before commencing the test marketing activity.

(c) *Recordkeeping.* Each person who is granted a TME must comply with the recordkeeping requirements of § 725.65. In addition, any person who obtains a TME must retain documentation of compliance with any restrictions imposed by EPA when it grants the TME. This information must be retained for 3 years from the final date of manufacture or import under the exemption.

### § 725.355 Information to be included in the TME application.

(a) To review a TME application, EPA must have sufficient information to permit a reasoned evaluation of the health and environmental effects of the planned test marketing activity. The person seeking EPA approval must submit all information known to or reasonably ascertainable by the submitter on the microorganism and the test marketing activity, including information not listed in paragraphs (c), (d), and (e) of this section that the person believes will demonstrate that the microorganism will not present an unreasonable risk of injury to health or the environment as a result of the test marketing. The TME application must be in writing and must include at least the information described in paragraphs (b), (c), (d), and (e) of this section.

(b) When specific information is not submitted, an explanation of why such information is not available or not applicable must be included.

(c) Persons applying for a TME must submit the submitter identification and microorganism identity information required for MCANs in § 725.155(c), (d)(1), and (d)(2).

(d) Persons applying for a TME must submit phenotypic and

ecological characteristics information required in § 725.155(d)(3) as it relates directly to the conditions of the proposed test marketing activity.

(e) Persons applying for a TME must also submit the following information about the proposed test marketing activity:

(1) *Proposed test marketing activity*. (i) The maximum quantity of the microorganism which the applicant will manufacture or import for test marketing.

(ii) The maximum number of persons who may be provided the microorganism during test marketing.

(iii) The maximum number of persons who may be exposed to the microorganism as a result of test marketing, including information regarding duration and route of such exposures.

(iv) A description of the test marketing activity, including its duration and how it can be distinguished from full-scale commercial production and research and development activities.

(2) *Health and environmental effects data*. All existing data regarding health and environmental effects of the microorganism must be reported in accordance with § 725.160.

### § 725.370 EPA review of the TME application.

General procedures for review of all submissions under this part are contained in § § 725.28 through 725.60. In addition, the following procedures apply to EPA review of TME applications submitted under this subpart:

(a) No later than 45 days after EPA receives a TME, the Agency will either approve or deny the application.

(b) A submitter may only proceed with test marketing activities after receipt of EPA approval.

(c) In approving a TME application, EPA may impose any restrictions necessary to ensure that the microorganism will not present an unreasonable risk of injury to health and the environment as a result of test marketing.

## Subpart G—Exemption for Microorganisms in General Commercial Use

### § 725.400 Scope and purpose.

(a) This subpart describes exemptions from reporting under subpart D of this part, and from review under this part altogether, for manufacturing and importing of certain new microorganisms for general commercial use.

(b) Recipient microorganisms eligible for the tiered exemption from review under this part are listed in § 725.420.

(c) Criteria for the introduced genetic material contained in the new microorganisms are described in § 725.421.

(d) Physical containment and control technologies are described in § 725.422.

(e) The conditions for the Tier I exemption are listed in § 725.424.

(f) In lieu of complying with subpart D of this part, persons using recipient microorganisms eligible for the tiered exemption may submit a Tier II exemption request. The limited reporting requirements for the Tier II exemption, including data requirements, are described in § § 725.450 and 725.455.

(g) EPA review procedures for the Tier II exemption are set forth in § 725.470.

(h) Subparts A through C of this part apply to any submission under this subpart.

### § 725.420 Recipient microorganisms.

The following recipient microorganisms are eligible for either exemption under this part:

(a) *Acetobacter aceti*.
(b) *Aspergillus niger*.
(c) *Aspergillus oryzae*.
(d) *Bacillus licheniformis*.
(e) *Bacillus subtilis*.
(f) *Clostridium acetobutylicum*.
(g) *Escherichia coli* K-12.
(h) *Penicillium roqueforti*.
(i) *Saccharomyces cerevisiae*.
(j) *Saccharomyces uvarum*.

### § 725.421 Introduced genetic material.

For a new microorganism to qualify for either exemption under this subpart, introduced genetic material must meet all of the criteria listed in this section.

(a) *Limited in size*. The introduced genetic material must consist only of the following:

(1) The structural gene(s) of interest.

(2) The regulatory sequences permitting the expression of solely the gene(s) of interest.

(3) Associated nucleotide sequences needed to move genetic material, including linkers, homopolymers, adaptors, transposons, insertion sequences, and restriction enzyme sites.

(4) The nucleotide sequences needed for vector transfer.

(5) The nucleotide sequences needed for vector maintenance.

(b) *Well characterized*. For introduced genetic material, well characterized means that the following have been determined:

(1) The function of all of the products expressed from the structural gene(s).

(2) The function of sequences that participate in the regulation of expression of the structural gene(s).

(3) The presence or absence of associated nucleotide sequences.

(c) *Poorly mobilizable*. The ability of the introduced genetic material to be transferred and mobilized is inactivated, with a resulting frequency of transfer of less than $10^{-8}$ transfer events per recipient.

(d) *Free of certain sequences*. The introduced genetic material must not contain any part of the nucleotide sequences that encode the toxins described in this paragraph (d). Although these toxins are listed according to the source organism, it is use of the nucleotide sequences that encode the toxins that are being restricted and not the use of the source organisms. The source organisms are listed to provide specificity in identification of sequences whose use is restricted. Similar or identical sequences may be isolated from organisms other than those listed below. Comparable toxin sequences, regardless of the organism from which they are derived, must not be included in the introduced genetic material. Toxin synonyms are included in parentheses.

(1) *Sequences for protein synthesis inhibitor.*

| | |
|---|---|
| *Corynebacterium diphtheriae & C. ulcerans* | Diphtheria toxin |
| *Pseudomonas aeruginosa* | Exotoxin A |
| *Shigella dysenteriae* | Shigella toxin (Shiga toxin, Shigella dysenteriae type I toxin, Vero cell toxin) |
| *Abrus precatorius*, seeds | Abrin |
| *Ricinus communis*, seeds | Ricin |

(2) *Sequences for neurotoxins.*

| | |
|---|---|
| *Clostridium botulinum* | Neurotoxins A, B, C1, D, E, F, G (Botulinum toxins, botulinal toxins) |
| *Clostridium tetani* | Tetanus toxin (tetanospasmin) |
| *Proteus mirabilis* | Neurotoxin |
| *Staphylococcus aureus* | Alpha toxin (alpha lysin) |
| *Yersinia pestis* | Murine toxin |
| Snake toxins | |
| *Bungarus caeruleus* | Caeruleotoxin |
| *Bungarus multicinctus* | Beta-bungarotoxin (phospholipase) |
| *Crotalus* spp. | Crotoxin (phospholipase) |
| *Dendroaspis viridis* | Neurotoxin |
| *Naja naja* varieties | Neurotoxin |
| *Notechia scutatus* | Notexin (phospholipase) |
| *Oxyuranus scutellatus* | Taipoxin |
| Invertebrate toxins | |
| *Chironex fleckeri* | Neurotoxin |
| *Androctnus australis* | Neurotoxin |
| *Centruroides sculpturatus* | Neurotoxin |

(3) *Sequences for oxygen labile cytolysins.*

| | |
|---|---|
| *Bacillus alve* | Alveolysin |
| *Bacillus cereus* | Cereolysin |
| *Bacillus laterosporus* | Laterosporolysin |
| *Bacillus thuringiensis* | Thuringiolysin |
| *Clostridium bifermentans* | Lysin |
| *Clostridium botulinum* | Lysin |
| *Clostridium caproicum* | Lysin |
| *Clostridium chauvoei* | Delta-toxin |
| *Clostridium histolyticum* | Epsilon-toxin |
| *Clostridium novyi* | Gamma-toxin |
| *Clostridium oedematiens* | Delta-toxin |
| *Clostridium perfringens* | Theta-toxin (Perfringolysin) |
| *Clostridium septicum* | Delta-toxin |
| *Clostridium sordellii* | Lysin |
| *Clostridium tetani* | Tetanolysin |
| *Listeria monocytogenes* | Listeriolysin (A B) |
| *Streptococcus pneumoniae* | Pneumolysin |
| *Streptococcus pyogene* | Streptolysin O (SLO) |

(4) *Sequences for toxins affecting membrane function.*

| | |
|---|---|
| *Bacillus anthracis* | Edema factor (Factors I II); Lethal factor (Factors II III) |
| *Bacillus cereus* | Enterotoxin (diarrheagenic toxin, mouse lethal factor) |
| *Bordetella pertussis* | Adenylate cyclase (Heat-labile factor); Pertussigen (pertussis toxin, islet activating factor, histamine sensitizing factor, lymphocytosis promoting factor) |
| *Clostridium botulinum* | C2 toxin |
| *Clostridium difficile* | Enterotoxin (toxin A) |
| *Clostridium perfringens* | Beta-toxin; Delta-toxin |
| *Escherichia coli* & other Enterobacteriaceae spp. | Heat-labile enterotoxins (LT); Heat-stable enterotoxins (STa, ST1 subtypes ST1a ST1b; also STb, STII) |
| *Legionella pneumophila* | Cytolysin |
| *Vibrio cholerae & Vibrio mimicus* | Cholera toxin (choleragen) |

(5) Sequences that affect membrane integrity.

| | |
|---|---|
| *Clostridium bifermentans* & other *Clostridium spp* | Lecithinase |
| *Clostridium perfringens* | Alpha-toxin (phospholipase C, lecithinase); Enterotoxin |
| *Corynebacterium pyogenes & other Corynebacterium spp.* | Cytolysin (phospholipase C), Ovis toxin (sphingomyelinase D) |
| *Staphylococcus aureus* | Beta-lysin (beta toxin) |

(6) *Sequences that are general cytotoxins.*

| | |
|---|---|
| *Adenia digitata* | Modeccin |
| *Aeromonas hydrophila* | Aerolysin (beta-lysin, cytotoxic lysin) |
| *Clostridium difficile* | Cytotoxin (toxin B) |
| *Clostridium perfringens* | Beta-toxin; Epsilon-toxin; Kappa-toxin |
| *Escherichia coli & other Enterobacteriaceae spp.* | Cytotoxin (Shiga-like toxin, Vero cell toxin) |
| *Pseudomonas aeruginosa* | Proteases |
| *Staphylococcus aureus* | Gamma lysin (Gamma toxin); Enterotoxins (SEA, SEB, SEC, SED SEE); Pyrogenic exotoxins A B; Toxic shock syndrome toxins (TSST-1) |
| *Staphylococcus aureus & Pseudomonas aeruginosa* | Leucocidin (leukocidin, cytotoxin) |
| *Streptococcus pyogenes* | Streptolysin S (SLS); Erythrogenic toxins (scarlet fever toxins, pyrogenic exotoxins) |
| *Yersinia enterocolitica* | Heat-stable enterotoxins (ST) |

**§ 725.422 Physical containment and control technologies.**

All of the following criteria for the physical containment and control technologies of the facility are required for a Tier I exemption and serve as guidance for a Tier II exemption:

(a) The structure is designed and operated to contain the microorganisms.

(b) Limit entry only to those persons whose presence is critical to the reliability or safety of the activity.

(c) Provide written, published, and implemented procedures for the safety of personnel and control of hygiene.

(d) Include inactivation procedures demonstrated and documented to be effective against the new microorganism contained in liquid and solid wastes prior to disposal of the wastes. The inactivation procedures must reduce microbial concentrations by at least 6 logs in liquid and solid wastes.

(e) Provide and document effectiveness of features to reduce microbial concentration by at least 2 logs in aerosols and exhaust gases released from the structure.

(f) Include and document systems for controlling dissemination of the microorganisms through other routes.

(g) Have in place emergency clean-up procedures.

**§ 725.424 Requirements for the Tier I exemption.**

(a) *Conditions of exemption.* The manufacture or import of a new microorganism for general commercial use is not subject to review under this part if all of the following conditions are met:

(1) The recipient microorganism is listed and meets any requirements specified in § 725.420.

(2) The introduced genetic material meets the criteria under § 725.421.

(3) The physical containment and control technologies of any facility in which the microorganism will be used meet the criteria under § 725.422.

(4) The manufacturer or importer submits a certification described in paragraph (b) of this section to EPA

30 days before commencing initial manufacture or import.

(5) The manufacturer or importer complies with the recordkeeping requirements of § 725.65 and maintains records that verify compliance with the following:

(i) The certifications made in paragraph (b) of this section.

(ii) All the eligibility criteria for the Tier I exemption including the criteria for the recipient microorganism, the introduced genetic material, the physical containment and control technologies.

(b) *Certification*. To be eligible for the exemption under this subpart, a manufacturer or importer must submit to EPA a document signed by a responsible company official containing the information listed in this paragraph.

(1) Name and address of manufacturer or importer.

(2) Date when manufacture or import is expected to begin.

(3) Certification of the following:

(i) The recipient microorganism is one of those listed in § 725.420

(ii) Compliance with the introduced genetic material criteria described in § 725.421.

(iii) Compliance with the containment requirements described in § 725.422, including the provision in paragraph (a)(3) of this section.

(4) The site of waste disposal and the type of permits for disposal, the permit numbers and the institutions issuing the permits.

(5) The certification statement required in § 725.25(b).

**§ 725.426 Liability of the manufacturer or importer who uses the Tier I exemption.**

The Tier I exemption under § 725.424 applies only to a manufacturer or importer of a new microorganism that certifies that the microorganism will be used in all cases in compliance with § § 725.420, 725.421, and 725.422.

**§ 725.428 Requirements for the Tier II exemption.**

The manufacturer or importer of a new microorganism for general commercial use may submit to EPA a Tier II exemption request in lieu of a MCAN under subpart D of this part if all of the following conditions are met:

(a) The recipient microorganism is listed and meets any requirements specified in § 725.420.

(b) The introduced genetic material meets the criteria under § 725.421.

(c) The criteria listed under § 725.422 for physical containment and control technologies of facilities should be used as guidance to satisfy the Tier II exemption request data requirements listed at § 725.455(d). EPA will review proposed process and containment procedures as part of the submission for a Tier II exemption under this section.

**§ 725.450 Procedural requirements for the Tier II exemption.**

General requirements for all submissions under this part are contained in § 725.25. In addition, the following requirements apply to requests submitted under this subpart:

(a) *Prenotice consultation*. EPA strongly suggests that for a Tier II exemption, the submitter contact the Agency for a prenotice consultation regarding eligibility for expedited review.

(b) *When to submit the Tier II exemption request*. Each manufacturer or importer who is eligible to submit a Tier II exemption request under this subpart must submit the request at least 45 calendar days before commencing manufacture or import.

(c) *Contents of the Tier II exemption request*. Each person who submits a request under this subpart must provide the information described in § § 725.428 and 725.455, as well as information sufficient to enable EPA to evaluate the effects of all activities described in the request.

(d) *Recordkeeping*. Each person who submits a request under this subpart must comply with the recordkeeping requirements of § 725.65. In addition, the submitter should maintain records which contain information that verifies compliance with the following:

(1) The certifications made in the request.

(2) All the eligibility criteria for the Tier II exemption request including the criteria for the recipient microorganism, the introduced genetic material, the physical containment and control technologies.

**§ 725.455 Information to be included in the Tier II exemption request.**

The applicant must indicate clearly that the submission is an Tier II exemption request for a microorganism instead of the MCAN under subpart D of this part and must submit the following information:

(a) *Submitter identification*. (1) The name and headquarters address of the submitter.

(2) The name, address, and office telephone number (including area code) of the principal technical contact representing the submitter.

(b) *Microorganism identity information*. (1) Identification (genus, species, and strain) of the recipient microorganism. Genus, species designation should be substantiated by a letter from a culture collection or a brief summary of the results of tests conducted for taxonomic identification.

(2) Type of genetic modification and the function of the introduced genetic material.

(3) Site of insertion.

(4) Certification of compliance with the introduced genetic material criteria described in § 725.421.

(c) *Production volume*. Production volume, including total liters per year, and the maximum cell concentration achieved during the production process.

(d) *Process and containment information*. (1) A description of the process including the following:

(i) Identity and location of the manufacturing site(s).

(ii) Process flow diagram illustrating the production process, including downstream separations, and indicating the containment envelope around the appropriate equipment.

(iii) Identities and quantities of feedstocks.

(iv) Sources and quantities of potential releases to both the workplace and environment, and a description of engineering controls, inactivation procedures, and other measures which will reduce worker exposure and environmental releases.

(v) A description of procedures which will be undertaken to prevent fugitive emissions, i.e. leak detection and repair program.

(vi) A description of procedures/ safeguards to prevent and mitigate accidental releases to the workplace and the environment.

(2) Certification of those elements of the containment criteria described in § 725.422 with which the manufacturer is in compliance, including stating by number the elements with which the manufacturer is in full compliance.

### § 725.470 EPA review of the Tier II exemption request.

General procedures for review of all submissions under this part are contained in § § 725.28 through 725.60. In addition, the following procedures apply to EPA review of requests submitted under this subpart:

(a) *Length of the review period.* The review period for the request will be 45 days from the date the Document Control Officer for the Office of Pollution Prevention and Toxics receives a complete request, or the date EPA determines the request is complete under § 725.33, unless the Agency extends the review period for good cause under § 725.56.

(b) *Criteria for review.* EPA will review the request to determine that the new microorganism complies with § 725.428 and that its use as described in the request will not present an unreasonable risk of injury to health or the environment.

(c) *EPA decision regarding the Tier II exemption request.* A decision concerning a request under this subpart will be made by the Administrator, or a designee.

(d) *Determination that the microorganism is ineligible for a Tier II review.* (1) EPA may determine that the manufacturer or importer is not eligible for Tier II review, because the microorganism does not meet the criteria under § 725.428 or the Administrator, or a designee, decides that there is insufficient information to determine that the conditions of use of the microorganism as described in the request will not present an unreasonable risk to health or the environment.

(2) If the Agency makes this determination, the Administrator, or a designee will notify the manufacturer by telephone, followed by a letter, that the request has been denied. The letter will explain reasons for the denial.

(3) If the request is denied, the manufacturer may submit the information necessary to constitute a MCAN under subpart D of this part.

(e) *Approval or denial of the Tier II exemption request.* (1) No later than 45 days after EPA receives a request, the Agency will either approve or deny the request.

(2) In approving a request, EPA may impose any restrictions necessary to ensure that the microorganism will not present an unreasonable risk of injury to health and the environment as a result of general commercial use.

(f) EPA may seek to enjoin the manufacture or import of a microorganism in violation of this subpart, or act to seize any microorganism manufactured or imported in violation of this section or take other actions under the authority of sections 7 or 17 of the Act.

## Subparts H–K—[Reserved]

## Subpart L—Additional Procedures for Reporting on Significant New Uses of Microorganisms

### § 725.900 Scope and purpose.

(a) This subpart describes additional provisions governing submission of MCANs for microorganisms subject to significant new use rules identified in subpart M of this part.

(b) Manufacturers, importers, and processors described in § 725.105(c) must submit a MCAN under subpart D of this part for significant new uses of microorganisms described in subpart M of this part, unless they are excluded under § § 725.910 and 725.912.

(c) Section 725.920 discusses exports and imports.

(d) Additional recordkeeping requirements specific to significant new uses of microorganisms are described in § 725.950.

(e) Section 725.975 describes how EPA will approve alternative means of complying with significant new use requirements designated in subpart M of this part.

(f) Expedited procedures for promulgating significant new use requirements under subpart M of this part for microorganisms subject to section 5(e) orders are discussed in § § 725.980 and 725.984.

### § 725.910 Persons excluded from reporting on significant new uses.

(a) A person who intends to manufacture, import, or process a microorganism identified in subpart M of this part and who intends to distribute it in commerce is not required to submit a MCAN under subpart D of this part, if that person can document one or more of the following as to each recipient of the microorganism from that person:

(1) That the person has notified the recipient, in writing, of the specific section in subpart M of this part which identifies the microorganism and its designated significant new uses.

(2) That the recipient has knowledge of the specific section in subpart M of this part which identifies the microorganism and its designated significant new uses.

(3) That the recipient cannot undertake any significant new use described in the specific section in subpart M of this part.

(b) The manufacturer, importer, or processor described in paragraph (a) of this section must submit a MCAN under subpart D of this part, if such person has knowledge at the time of commercial distribution of the microorganism identified in the specific section in subpart M of this part that a recipient intends to engage in a designated significant new use of

that microorganism without submitting a MCAN under this part.

(c) A person who processes a microorganism identified in a specific section in subpart M of this part for a significant new use of that microorganism is not required to submit a MCAN if that person can document each of the following:

(1) That the person does not know the specific microorganism identity of the microorganism being processed.

(2) That the person is processing the microorganism without knowledge that the microorganism is identified in subpart M of this part.

(d)(1) If at any time after commencing distribution in commerce of a microorganism identified in a specific section in subpart M of this part, a person who intends to manufacture, import, or process a microorganism described in subpart M of this part and intends to distribute it in commerce has knowledge that a recipient of the microorganism is engaging in a significant new use of that microorganism designated in that section without submitting a MCAN under this part, the person is required to cease supplying the microorganism to that recipient and to submit a MCAN for that microorganism and significant new use, unless the person is able to document each of the following:

(i) That the person has notified the recipient and EPA enforcement authorities (at the address in paragraph (d)(1)(iii) of this section), in writing within 15 working days of the time the person develops knowledge that the recipient is engaging in a significant new use, that the recipient is engaging in a significant new use without submitting a MCAN.

(ii) That, within 15 working days of notifying the recipient as described in paragraph (d)(1)(i) of this section, the person received from the recipient, in writing, a statement of assurance that the recipient is aware of the terms of the applicable section in subpart M of this part and will not engage in the significant new use.

(iii) That the person has promptly provided EPA enforcement authorities with a copy of the recipient's statement of assurance described in paragraph (d)(1)(ii) of this section. The copy must be sent to the Director, Office of Compliance Monitoring (EN–342), Environmental Protection Agency, 401 M St., SW., Washington, DC 20460.

(2) If EPA notifies the manufacturer, importer, or processor that the recipient is engaging in a significant new use after providing the statement of assurance described in paragraph (d)(1)(ii) of this section and without submitting a MCAN under this part, the manufacturer, importer, or processor shall immediately cease distribution to that recipient until the manufacturer, importer, or processor or the recipient has submitted a MCAN under this part and the MCAN review period has ended.

(3) If, after receiving a statement of assurance from a recipient under paragraph (d)(1)(ii) of this section, a manufacturer, importer, or processor has knowledge that the recipient is engaging in a significant new use without submitting a MCAN under this part, the manufacturer, importer, or processor must immediately cease distributing the microorganism to that recipient and notify EPA enforcement authorities at the address identified in paragraph (c)(1)(iii) of this section. The manufacturer, importer, or processor may not resume distribution to that recipient until any one of the following has occurred:

(i) The manufacturer, importer, or processor has submitted a MCAN under this part and the MCAN review period has ended.

(ii) The recipient has submitted a MCAN under this part and the MCAN review period has ended.

(iii) The manufacturer, importer, or processor has received notice from EPA enforcement authorities that it may resume distribution to that recipient.

### § 725.912 Exemptions.

Persons identified in § § 725.100(c) and 725.910 are not required to submit a MCAN under subpart D of this part for a microorganism identified in subpart M of this part, unless otherwise specified in a specific section in subpart M, if:

(a) The person submits a MCAN for the microorganism prior to the promulgation date of the section in subpart M of this part which identifies the microorganism, and the person receives written notification of compliance from EPA prior to the effective date of such section. The MCAN submitter must comply with any applicable requirement of section 5(b) of the Act. The MCAN must include the information and test data specified in section 5(d)(1) of the Act. For purposes of this exemption, the specific section in subpart M of this part which identifies the microorganism and § § 725.3, 725.15, 725.65, 725.70, 725.75, 725.100, and 725.900 apply; after the effective date of the section in subpart M of this part which identifies the microorganism, § § 725.105 and 725.910 apply and § 725.920 continues to apply. EPA will provide the MCAN submitter with written notification of compliance only if one of the following occurs:

(1) EPA is unable to make the finding that the activities described in the MCAN will or may present an unreasonable risk of injury to health or the environment under reasonably foreseeable circumstances.

(2) EPA and the person negotiate a consent order under section 5(e) of the Act, such order to take effect on the effective date of the section in subpart M of this part which identifies the microorganism.

(b) The person is operating under the terms of a consent order issued under section 5(e) of the Act applicable to that person. If a provision of such section 5(e) order is inconsistent with a specific significant new use identified in subpart M of this part, abiding by the provision of the section 5(e) order exempts the person from submitting

a MCAN for that specific significant new use.

### § 725.920 Exports and imports.

(a) *Exports*. Persons who intend to export a microorganism identified in subpart M of this part, or in any proposed rule which would amend subpart M of this part, are subject to the export notification provisions of section 12(b) of the Act. The regulations that interpret section 12(b) appear at 40 CFR part 707.

(b) *Imports*. Persons who import a substance identified in a specific section in subpart M of this part are subject to the import certification requirements under section 13 of the Act, which are codified at 19 CFR § § 12.118 through 12.127 and 12.28. The EPA policy in support of the import certification requirements appears at 40 CFR part 707.

### § 725.950 Additional recordkeeping requirements for reporting of significant new uses.

Persons submitting a MCAN for a significant new use of a microorganism must comply with the recordkeeping requirements of § 725.65. In addition, the following requirements apply:

(a) At the time EPA adds a microorganism to subpart M of this part, the Agency may specify appropriate recordkeeping requirements. Each manufacturer, importer, and processor of the microorganism shall maintain the records for 3 years from the date of their creation.

(b) The records required to be maintained under this section may include the following:

(1) Records documenting the information contained in the MCAN submitted to the Agency.

(2) Records documenting the manufacture and importation volume of the microorganism and the corresponding dates of manufacture and import.

(3) Records documenting volumes of the microorganism purchased domestically by processors of the microorganism, names and addresses of suppliers and corresponding dates of purchase.

(4) Records documenting the names and addresses (including shipment destination address, if different) of all persons outside the site of manufacture or import to whom the manufacturer, importer, or processor directly sells or transfers the microorganism, the date of each sale or transfer, and the quantity of the microorganism sold or transferred on such date.

### § 725.975 EPA approval of alternative control measures.

(a) In certain sections of subpart M of this part, significant new uses for the identified microorganisms are described as the failure to establish and implement programs providing for the use of either: specific measures to control worker exposure to or release of microorganisms which are identified in such sections, or alternative measures to control worker exposure or environmental release which EPA has determined provide substantially the same degree of protection as the specified control measures. Persons who manufacture, import, or process a microorganism identified in such sections and who intend to employ alternative measures to control worker exposure or environmental release must submit a request to EPA for a determination of equivalency before commencing manufacture, import, or processing involving the alternative control measures.

(b) A request for a determination of equivalency must be submitted in writing to the Office of Pollution Prevention and Toxics, Document Control Officer, 7407, 401 M St., SW., Washington, DC 20460: ATTN: SNUR Equivalency Determination, and must contain:

(1) The name of the submitter.

(2) The specific identity of the microorganism.

(3) The citation for the specific section in subpart M of this part which pertains to the microorganism for which the request is being submitted.

(4) A detailed description of the activities involved.

(5) The specifications of the alternative worker exposure control measures or environmental release control measures.

(6) An analysis justifying why such alternative control measures provide substantially the same degree of protection as the specific control measures identified in the specific section in subpart M of this part which pertains to the microorganism for which the request is being submitted.

(7) The data and information described in § § 725.155 and 725.160 of this part unless such data and information have already been submitted to EPA's Office of Pollution Prevention and Toxics.

(c) Requests for determinations of equivalency will be reviewed by EPA within 45 days. Determinations under this paragraph will be made by the Director, or a designee. Notice of the results of such determinations will be mailed to the submitter.

(d) If EPA notifies the submitter under paragraph (c) of this section that EPA has determined that the alternative control measures provide substantially the same degree of protection as the specified control measures identified in the specific section of subpart M of this part which pertains to the microorganism for which the request is being submitted, the submitter may commence manufacture, import, or processing in accordance with the specifications for alternative worker exposure control measures or environmental release control measures identified in the submitter's request, and may alter any corresponding notification to workers to reflect such alternative controls. Deviations from the activities described in the EPA notification constitute a significant new use and are subject to the requirements of this part.

### § 725.980 Expedited procedures for issuing significant new use rules for microorganisms subject to section 5(e) orders.

(a) *Selection of microorganisms*. (1) In accordance with the expedited process specified in this section, EPA will issue significant new use

notification requirements for each new microorganism that, after MCAN review under subpart D of this part, becomes subject to a final order issued under section 5(e) of the Act, except for an order that prohibits manufacture and import of the microorganism, unless EPA determines that significant new use notification requirements are not needed for the microorganism.

(2) If EPA determines that significant new use notifications requirements are not needed for a microorganism that is subject to a final order issued under section 5(e) of the Act, EPA will issue a notice in the **Federal Register** explaining why the significant new use requirements are not needed.

(b) *Designation of requirements*. (1) The significant new use notification and other specific requirements will be based on and be consistent with the provisions included in the final order issued for the microorganism under section 5(e) of the Act. EPA may also designate additional activities as significant new uses which will be subject to notification.

(2) Significant new use requirements and other specific requirements designated under this section will be listed in subpart M of this part. For each microorganism, subpart M of this part will identify:

(i) The microorganism name.

(ii) The activities designated as significant new uses.

(iii) Other specific requirements applicable to the microorganism, including recordkeeping requirements or any other requirements included in the final section 5(e) order.

(c) *Procedures for issuing significant new use rules*. (1) Possible processes. EPA will issue significant new use rules under this section by one of the following three processes: direct final rulemaking, interim final rulemaking, or notice and comment rulemaking. EPA will use the direct final rulemaking process to issue significant new use rules unless it determines that, in a particular case, one of the other processes is more appropriate.

(2) Notice in the **Federal Register**. **Federal Register** documents issued to propose or establish significant new uses under this section will contain the following:

(i) The microorganism identity or, if its specific identity is claimed confidential, an appropriate generic microorganism name and an accession number assigned by EPA.

(ii) The MCAN number.

(iii) A summary of EPA's findings under section 5(e)(1)(A) of the Act for the final order issued under section 5(e).

(iv) Designation of the significant new uses subject to, or proposed to be subject to, notification and any other applicable requirements.

(v) Any modification of subpart M of this part applicable to the specific microorganism and significant new uses.

(vi) If the **Federal Register** document establishes a final rule, or notifies the public that a final rule will not be issued after public comment has been received, the document will describe comments received and EPA's response.

(3) *Direct final rulemaking*. (i) EPA will use the direct final rulemaking procedure to issue a significant new use rule, when specific requirements will be based on and be consistent with the provisions included in the final order issued for the microorganism under section 5(e) of the Act. The Agency will issue a final rule in the **Federal Register** following its decision to develop a significant new use rule under this section for a specific new microorganism.

(ii) The **Federal Register** document will state that, unless written notice is received by EPA within 30 days of publication that someone wishes to submit adverse or critical comments, the rule will be effective 60 days from the date of publication. The written notice of intent to submit adverse or critical comments should state which SNUR(s) will be the subject of the adverse or critical comments, if several SNURs are established through the direct final rule. If notice is received within 30 days that someone wishes to submit adverse or critical comments, the section(s) of the direct final rule containing the SNUR(s) for which a notice of intent to comment was received will be withdrawn by EPA issuing a document in the final rule section of the **Federal Register**, and a proposal will be published in the proposed rule section of the **Federal Register**. The proposal will establish a 30–day comment period.

(iii) If EPA, having considered any timely comments submitted in response to the proposal, decides to establish notification requirements under this section, EPA will issue a final rule adding the microorganism to subpart M of this part and designating the significant new uses subject to notification.

(4) *Interim final rulemaking*. (i) EPA will use the interim final rulemaking procedure to issue a significant new use rule, when specific requirements will be based on and be consistent with the provisions included in the final order issued for the microorganism under section 5(e) of the Act. The Agency will issue an interim final rule in the **Federal Register** following its decision to develop a significant new use rule for a specific new microorganism. The document will state EPA's reasons for using the interim final rulemaking procedure.

(A) The significant new use rule will take effect on the date of publication.

(B) Persons will be given 30 days from the date of publication to submit comments.

(ii) Interim final rules issued under this section shall cease to be in effect 180 days after publication unless, within the 180–day period, EPA issues a final rule in the **Federal Register** responding to any written comments received during the 30–day comment period specified in paragraph (c)(5)(i)(B) of this section and promulgating final significant new use notification requirements and other requirements for the microorganism.

(5) *Notice and comment rulemaking*. (i) EPA will use a notice and comment procedure to issue a significant new use rule, when EPA is designating additional activities which are not provisions included in the final order issued for the microorganism under section 5(e) of the Act as significant new uses which will be subject to notification. EPA will issue a proposal in the **Federal Register** following its decision to develop a significant new use rule under this section for a specific new microorganism. Persons will be given 30 days to comment on whether EPA should establish notification requirements for the microorganism under this part.

(ii) If EPA, having considered any timely comments, decides to establish notification requirements under this section, EPA will issue a final rule adding the microorganism to subpart M of this part and designating the significant new uses subject to notification.

(d) *Schedule for issuing significant new use rules*. (1) Unless EPA determines that a significant new use rule should not be issued under this section, EPA will issue a proposed rule, a direct final rule, or an interim final rule within 180 days of receipt of a valid notice of commencement under § 725.190 of this part.

(2) If EPA receives adverse or critical significant comments following publication of a proposed or interim final rule, EPA will either withdraw the rule or issue a final rule addressing the comments received.

### § 725.984 Modification or revocation of certain notification requirements.

(a) *Criteria for modification or revocation*. EPA may at any time modify or revoke significant new use notification requirements for a microorganism which has been added to subpart M of this part using the procedures of § 725.980. Such action may be taken under this section if EPA makes one of the following determinations, unless other information shows that the requirements should be retained:

(1) Test data or other information obtained by EPA provide a reasonable basis for concluding that activities designated as significant new uses of the microorganism will not present an unreasonable risk of injury to health or the environment.

(2) EPA has promulgated a rule under section 4 or 6 of the Act, or EPA or another agency has taken action under another law, for the microorganism that eliminates the need for significant new use notification under section 5(a)(2) of the Act.

(3) EPA has received MCANs for some or all of the activities designated as significant new uses of the microorganism and, after reviewing such MCANs, concluded that there is no need to require additional notice from persons who propose to engage in identical or similar activities.

(4) For a microorganism added to subpart M of this part under § 725.980, EPA has examined new information, or has reexamined the test data or other information supporting its finding under section 5(e)(1)(A)(ii)(I) of the Act and has concluded that a rational basis no longer exists for the findings that activities involving the microorganism may present an unreasonable risk of injury to human health or the environment required under section 5(e)(1)(A) of the Act.

(5) For a microorganism added to subpart M of this part under § 725.980, certain activities involving the microorganism have been designated as significant new uses pending the completion of testing, and adequate test data developed in accordance with applicable procedures and criteria have been submitted to EPA.

(b) Procedures for limitation or revocation. Modification or revocation of significant new use notification requirements for a microorganism that has been added to subpart M of this part using the procedures described in § 725.980 may occur either at EPA's initiative or in response to a written request.

(1) Any affected person may request modification or revocation of significant new use notification requirements for a microorganism that has been added to subpart M of this part using the procedures described in § 725.980 by writing to the Director, or a designee, and stating the basis for such request. The request must be accompanied by information sufficient to support the request. All requests should be sent to the TSCA Document Processing Center (7407), Room L–100, U.S. Environmental Protection Agency, 401 M St., SW., Washington, DC 2O46O, ATTN: Request to amend SNUR.

(2) The Director, or a designee, will consider the request, make a determination whether to initiate rulemaking to modify the requirements, and notify the requester of that determination by certified letter. If the request is denied, the letter will explain why EPA has concluded that the significant new use notification requirements for that microorganism should remain in effect.

(3) If EPA concludes that significant new use notification requirements for a microorganism should be limited or revoked, EPA will propose the changes in a notice in the **Federal Register**, briefly describe the grounds for the action, and provide interested parties an opportunity to comment.

## Subpart M—Significant New Uses for Specific Microorganisms—[Reserved]

[FR Doc. 94–21359 Filed 8–31–94; 8:45 am]

**BILLING CODE 6560–50–F**